AN ANALYSIS OF MULTIPLE VARIABLES ASSOCIATED WITH EXERCISE-INDUCED OLIGO-AMENORRHEA

by

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SUPERVISORY COMMITTEE APPROVAL

of a dissertation submitted by

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This dissertation has been read by each member of the following supervisory committee and by majority vote has been found to be satisfactory.

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FINAL READING APPROVAL

To the Graduate Council of The University of Utah:

I have read the dissertation of D. Patricia [redacted] in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the Supervisory Committee and is ready for submission to the Graduate School.

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ABSTRACT

A study of the relationships among multiple variables associated with exercise-induced oligo-amenorrhea in 70 healthy female runners, 18-37 years of age, was conducted. Seventy-seven percent of the runners were eumenorrheic while 23% were oligo-amenorrheic. The purpose of the study was to examine the relationship among serum lipids, body fat and ovarian hormones as well as re-examine other variables previously cited in the literature as being associated with exercise-induced amenorrhea, using multiple correlation and regression analysis. All participants completed a running and menstrual history questionnaire, the Schedule of Recent Experiences questionnaire, a four day diet diary, submaximal treadmill test, skinfold thicknesses, height and weight measurements and had two blood samples taken for analysis of estradiol, testosterone, progesterone and serum lipids.

Analysis of the data revealed statistically significant zero-order correlations between the number of menstrual cycles per year and predicted maximum oxygen uptake, training time per mile, percent body fat, nutritional intake, and serum estradiol levels. Multiple regression analysis revealed that only 12% of the variation in serum estradiol was explained by age, cholesterol intake, serum cholesterol, HDL cholesterol and percent body fat. A path

analysis was utilized to explore possible causal linkages between variables of interest; 41% of the variation in the number of menstrual cycles per year was explained by the variables used in the path diagram. The mechanisms through which body fat, cholesterol intake and serum cholesterol affect the number of menstrual cycles per year remains to be elucidated.

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* * * * * * * * * *

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CHAPTER I

INTRODUCTION

The changing focus and awareness of society concerning the needs and capabilities of women has resulted in many alterations in lifestyle for women in the past fifteen years, one of which is a growing involvement in participatory sport and exercise activities. This growth has been augmented by recent interest of society in preventive health measures and in exercise as a means of achieving an improved health status. Because increasing numbers of women are choosing to become involved in vigorous sports and exercise activities, the numbers of women who experience health related problems with participation are increasing and coming to the attention of health professionals more frequently. In particular, women have noted the onset of alterations in their menstrual cycles, especially oligomenorrhea and secondary amenorrhea. In studies that have been reported, secondary amenorrhea has been documented as occurring at a much higher rate in women who participate in regular vigorous exercise programs than in the average, more sedentary, population of women (Erdelyi, 1962; Erdelyi, 1976; Feicht, Johnson, Martin, Sparkes & Wagner, 1978; Carlberg & Riedesel, 1979; Dale, Gerlach & Wilhite, 1979; Baker Mathur, Kirk & Williamson, 1981; Lutter & Cushman, 1982).

The American College of Sports Medicine (1979) reports that approximately one third of competitive female long-distance runners ages 12 to 45, experience oligomenorrhea or secondary amenorrhea. Thus, studies over the past 15 years have shown that vigorous exercise, particularly running, is potentially a contributing factor in the development of menstrual irregularity.

Statement of the Problem

The etiologies of this higher rate of secondary amenorrhea in women runners and the factors associated with its development have not been clearly identified or evaluated. In the studies that have been done, the physiological and psychological stress of running, prior reproductive history and changes in percent body fat since beginning to run are most frequently postulated as being responsible, either separately or in combination, for the alterations in menstrual patterns which occur in some runners (Baker, 1981). The effects of physical training, particularly running, on ovarian hormone levels (Dale, Gerlach & Wilhite, 1979a; Shangold, Freeman, Thysen & Gatz, 1979; Baker et al., 1981) and on stored body fat and serum lipids (Adams, 1972; Wood, Haskell, Stern, Lewis & Perry, 1977; Dale, Gerlach, Martin & Alexander, 1979b; Miller, Rao & Lewis, 1979) have been documented. There is also a relationship between lipids and ovarian hormones: stored body lipids act as a site for peripheral estrogen synthesis; cholesterol is a precursor for estrogen synthesis; and lipoproteins act as carrier molecules for estrogen (Tepperman, 1980; Siiteri & Febres, 1980).

It is not known, however, what the specific effects of physical training, particularly running, are, on the relationships among serum lipids, body composition and reproductive hormones in the female and how these factors may interact to contribute to the development of oligomenorrhea or secondary amenorrhea in women runners.

The purpose of this study was to examine the relationships among serum lipids, body composition and ovarian hormones in the physically conditioned female. The relationships among variables cited in the literature as being associated with exercise-induced amenorrhea were also re-examined utilizing multiple correlation and regression analysis. The previously cited variables under consideration included age at the time of the study, prior menstrual history, percent body fat, body weight, weight loss, and training intensity. Variables not previously evaluated in published reports but considered in this study included nutritional factors, life stress and running associated stress. The information resulting from this study will contribute to the understanding of the variables associated with exercise-induced oligomenorrhea and amenorrhea in women runners, expanding the base of knowledge from which health professionals may advise clients concerning exercise and its potential risks. As an extension of the work completed by Dale et al. (1979 a), this study will also form the basis for future longitudinal investigation into the development of secondary amenorrhea in women runners.

CHAPTER II

REVIEW OF LITERATURE

The literature relative to this subject includes what is known about the control and regulation of the menstrual cycle and what is known about factors, particularly exercise, which may cause alterations in the menstrual cycle.

Control and Regulation of the Menstrual Cycle

Control of the menstrual cycle depends upon complex interactions among the hypothalamus, the anterior pituitary and the ovaries. The hypothalamus and the anterior pituitary act as a unit to release the gonadotropin hormones which lead to follicular maturation and associated cellular production of estrogen in the ovary. The estrogens produced in the ovary then exert a feedback signal necessary to achieve the appropriate release of gonadotropin hormones. The interrelationships are indicated in Figure 1. Not only is the timing of release of the various hormones important in achieving ovulation, but also the hormones must be released in sufficient amounts and the target organs must be receptive to hormonal stimulation (Yen, 1979). Summarized in Figure 2 are the circulating hormone levels during ovarian and endometrial events in the human female. The hormones apparently most important in

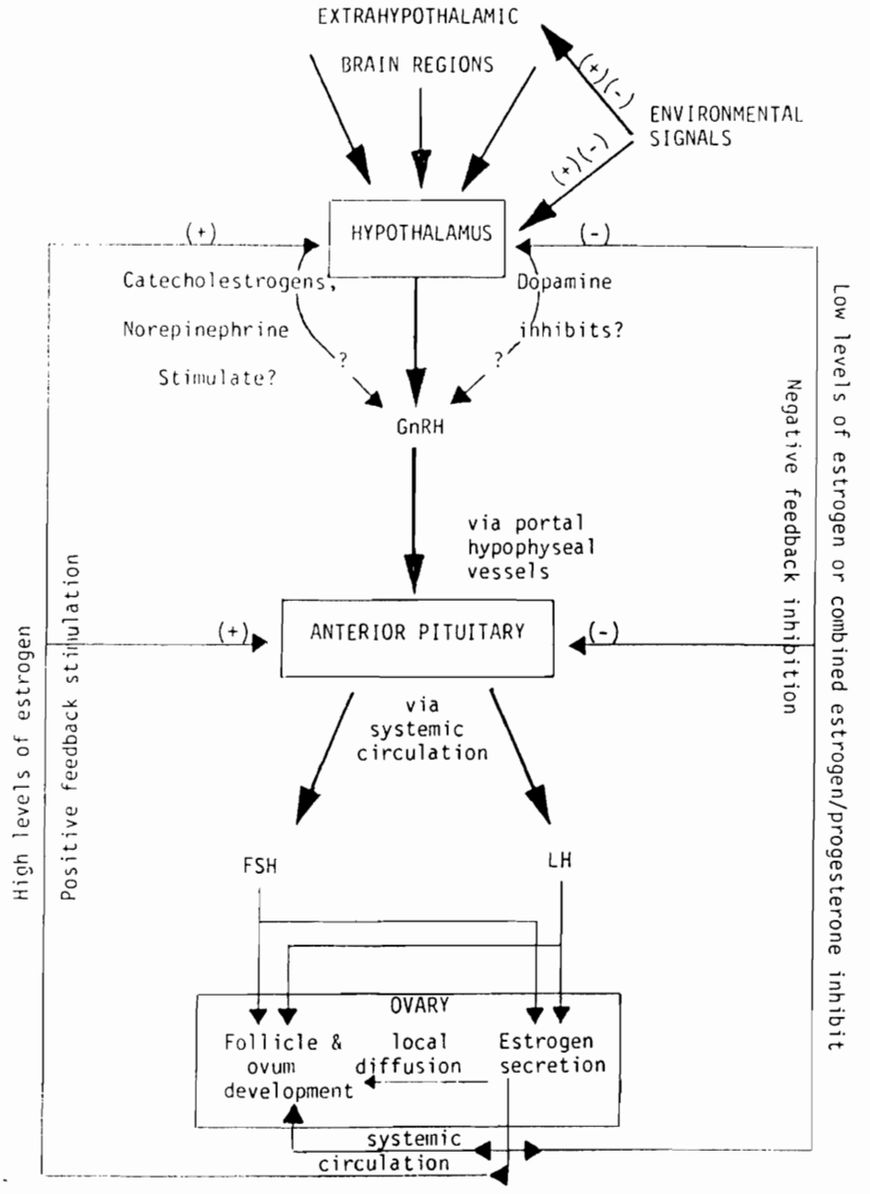

Figure 1. Control of the menstrual cycle. (Adapted from Ruch & Patton, 1979; Vander, Sherman & Luciano, 1980)

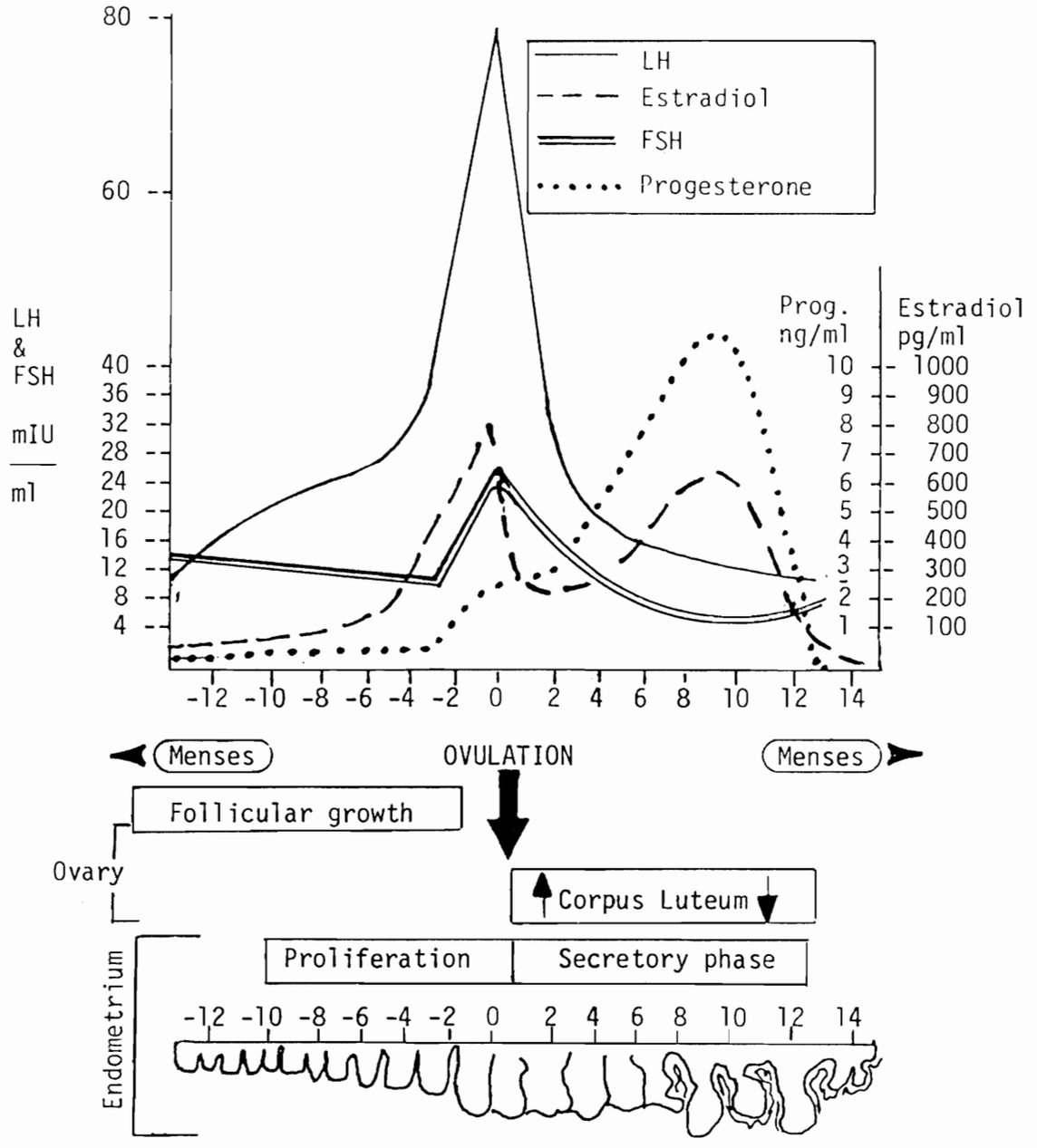

Figure 2. Events of the menstrual cycle. A summary of circulating hormone levels during ovarian and endometrial events in the human being (Adapted from Tepperman, 1980, p. 131).

exerting feedback control are the ovarian hormones, estrogen and progesterone. A chart summarizing the feedback influences of these hormones appears in Table 1.

Control of the hypothalamus and the release of GnRH to stimulate the pituitary is not clearly understood at present. The feedback influence of estrogen and perhaps LH have been noted in the literature (Ruch & Patton, 1979; Yen, 1979; Tepperman, 1980). In addition, neurotransmitters which are involved with GnRH release have been under recent investigation. Serotonin, dopamine, norepinephrine, acetycholine and gamma amino butyric acid have all been investigated. A tentative scheme which is finding increasing support is one proposed by Yen: norepinephrine and dopamine have opposing effects on GnRH, norepinephrine stimulates and dopamine inhibits.

In addition, a new class of compounds called catecholestrogens has been discovered in the hypothalamus and pituitary. These compounds are formed from estrogen by brain tissue as described by Fishman and Norton (1975). These catecholestrogens (See Figure 3) demonstrate no estrogenic activity by usual bioassay methods. Their structural similarity to catecholamines in the brain area are so close that they are metabolized by the same enzymes. The role of these compounds in the feedback regulation of GnRH release is not presently known, although Tepperman (1980) and Yen (1979) postulated that they may function as antiestrogens in which case they could block out the feedback inhibitory effects of estrogens

Table 1

Summary of Important Feedback Effects of Estrogen and Progesterone

Estrogen
In low plasma concentrations, inhibits the hypothalamic neurons which secrete GnRH and the anterior pituitary cells which secrete FSH. In high plasma concentrations, stimulates the hypothalamic neurons which secrete GnRH and the anterior pituitary cells which secrete LH.
Estrogen and Progesterone
Inhibit the hypothalamic neurons which secrete GnRH and possibly inhibit the anterior pituitary as well

Note. Adapted from Mountcastle, 1980.

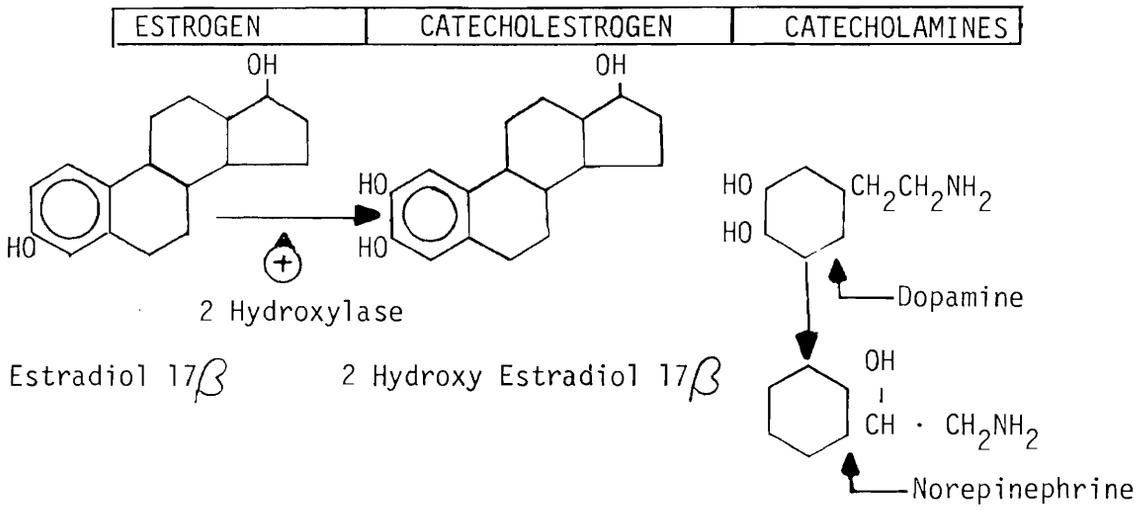

Figure 3. Catecholestrogens and their relation to catecholamines. (Adapted from Tepperman, 1980).

and facilitate GnRH release.

The pituitary gland, through its secretion of FSH and LH, is involved in the control of the menstrual cycle. The rates of secretion appear to depend directly on secretion of GnRH by the hypothalamus and on systemic estrogen levels. Estrogen, at low levels in the early follicular phase, has a direct inhibitory effect on the anterior pituitary cells which secrete FSH. This action accounts for the fact that FSH and LH secretion are not completely parallel during this phase, as would be expected with only one releasing factor for the two gonadotropins. In the late follicular phase, there are increasing levels of estrogen; this has a direct effect on the anterior pituitary cells which secrete LH, causing the mid-cycle surge of LH. The effect of rising estrogen and progesterone levels in the luteal phase may have some direct inhibitory effect on the anterior pituitary cells.

Factors Other Than Exercise Which Cause Variation in Reproductive Hormone Levels and Their Regulation of the Menstrual Cycle

Many aspects of the menstrual cycle are variable for individuals, particularly the length of each cycle and the age at which menarche and menopause occur. Zacharias, Wurlman and Schatzoff (1970) reviewed the literature concerning factors influencing age at menarche. They discussed the population dependent variation in age at menarche as well as time dependent changes. For example, in the United States the mean age of menarche in 1932 was 13.5

years while in 1968 it was noted to be 12.8 years. They also observed that age at menarche is susceptible to modification by factors such as nutrition and living conditions. They noted that specific physiological disorders altered the age of onset of menarche, including diabetes mellitus, blindness and obesity.

The "critical fat" hypothesis proposed by Frisch and MacArthur (1974) postulated that attainment of a critical percentage of body fat is necessary before menarche will occur. Their study indicated that in females with 22 to 30% body fat, menarche was experienced at a significantly younger age and that women with less than 22% body fat had either delayed or very irregular menstrual patterns. Siiteri and Febres (1980) suggested that if this hypothesis is substantiated, it may be because peripheral estrogen formation from androgen which takes place in fat may "prime" the hypothalamus, the pituitary, or even the ovaries to initiate cyclic functions. However, the mechanisms for the initiation of the menstrual cycle remain speculative at present.

For many years, the length of the menstrual cycle had been associated by folklore to the duration of the lunar cycle. There is no evidence to support this. Studies have shown that the majority of cycles are between 25 and 30 days in length with the distribution skewed towards cycles of 30 days. The greatest variability is seen in the year following menarche and the years immediately preceding menopause. During these times, the cycle length is significantly increased mainly because of the frequency

of anovulation and of prolonged follicular phases. The smallest variability occurs between the ages of 20 and 30. The secretory or luteal phase in menstrual cycles has been noted to be remarkably constant in duration, lasting 11 to 14 days while the length of the follicular phase is much more variable, lasting from 4 to 20 days. The correlation between the length of two consecutive cycles is poor. For example, it has been calculated that the proportion of subsequent cycles that fell in the range of past cycles averaged 64% when based on the range of the past three cycles but 90% when based on the range of the past 12 cycles (Ruch & Patton, 1979).

Once the menstrual cycle has been established, it is known that several factors cause variation in the length of the cycles. Stress has been studied extensively, particularly in animals and is highly correlated with variations in the length of the menstrual cycle. It is proposed that stress has a dual action on the hypothalamus and pituitary, resulting in decreased levels of pituitary gonadotropins (Vander et al., 1980). The effect of light in altering the length of the menstrual cycle has been well documented and is probably due to the influence of the hypothalamus. The effects of noise and olfactory stimuli on reproductive function have been documented best in animal studies. Female rats and rabbits were subjected to continuous, intense sound from an alarm bell. Initially, there was no noticeable effect on behavior, however, after 14 days rats demonstrate ovarian and uterine hypertrophy with increased LH levels. Olfactory studies in animals indicated that female mice, if isolated

from male mice, have irregular or anovulatory cycles. Introduction of a male or male scent to the females was effective in restoring normal LH fluctuations. As noted in Figure 1, these fluctuations tend to emphasize the effects of extero-receptive stimuli on the hypothalamus (Williams, 1980).

A factor which significantly alters the production of gametes and may alter the hypothalamic-pituitary axis is the use of oral contraceptives. Commonly used steroid contraceptives consist of synthetic estrogens (ethinyl, estradiol, or mestranol) in combination with progestogens derived from 19-nortestosterone or 17-hydroxy progesterone. The agents may interfere with fertility by disturbing function at the following loci: a) hypothalamus-pituitary-gonadotropin secreting apparatus, b) the ovary, c) the fallopian tubes, d) sperm transport to the site of fertilization, e) endometrium and/or f) cervical secretory glands. Estrogens may interfere with follicular development by inhibiting FSH release, and estrogens, and progestogens may inhibit the ovulatory surge of gonadotropins presumably by acting at the hypothalamic level and possibly by direct action on the pituitary. Some may directly affect the ovary, inhibiting steroidogenesis. "Low dose" pills may suppress fertility, even when permitting ovluation, by rendering the endometrium unsuitable for nidation; by altering the transit time of the ovum through the fallopian tubes or causing a thickening of cervical mucus making the cervix impermeable to sperm. These effects are usually reversible, with normal menstrual cycles returning within approximately three months after discontinuing the medication (Tepperman, 1980).

Studies have shown that the incidence of post-pill amenorrhea is very small, from 0.2% to 2.2% (Larsson-Cohn, 1969; Evrard, Buxton & Eriksen, 1976).

Other factors occur in healthy females which significantly affect the menstrual cycle and cause more severe variations in the cycle. The most extreme of those variations is the development of secondary amenorrhea. The most frequent cause of secondary amenorrhea in normal females is pregnancy. It is of interest to note that after pregnancy, some maturing of the human reproductive system is thought to occur leading to a regular menstrual pattern after pregnancy, even if this was not the pattern prior to pregnancy (Williams, 1980). Post-pregnancy lactation is also reported to be a cause of secondary amenorrhea (Harrison, 1974).

Secondary amenorrhea does occur in women who are not pregnant and who have no known pathological or disease states. A postal survey of 1,862 women in Sweden was designed to collect data regarding the occurrence of secondary amenorrhea of more than three months duration and of social factors associated with secondary amenorrhea. The social factors included marital status, area of residence and smoking habits. Of the respondents, 3.3% (62) had secondary amenorrhea not due to pregnancy or surgical treatment. It appeared from a simple analysis that prevalence rates were low in women 25-39 years of age, in married as compared to single women, in women living in provincial areas as compared to cities, in nonsmokers as compared to smokers or ex-smokers. Nulliparous women and those with later menarche had a higher prevalence rate than those who had

given birth or had menarche later in life. The multi-factorial analysis of these factors showed that they offered very low explanatory power with the exception of age. The association with age may be explained by the occurrence of women in the postmenopausal phases in the older group (Petterson, Fries & Nillus, 1973). This study did not attempt to evaluate the two factors most frequently associated with secondary amenorrhea, weight loss and stress. The 3.3% of unexplained secondary amenorrhea is comparable to the 6.0% incidence of secondary amenorrhea noted in U.S. college females by G. Betz (Feicht et al., 1978).

Frisch's "critical fat hypothesis," mentioned earlier, addresses weight change as indicated by body fat, and its relationship to the maintenance of menstrual cycles. Frisch and MacArthur's study (1974) showed that 22% of body weight is the minimal fat content required for the maintenance of menstrual cycles for women of ages 16 and older. This number was derived using percentiles of total water/body weight percentile, which are percentiles of "fatness." Their study further showed that weight changes in the range of ten to fifteen percent of total body weight are associated with the development and reversing of secondary amenorrhea. Frisch stated that weight loss or gain of this magnitude is mainly loss or gain of fat which suggests that a minimum level of stored, easily mobilized energy is necessary for ovulation and menstrual cycles in the female. These standards developed by Frisch apply only to Caucasian U.S. females and European females. Frisch also considered that other factors, such as emotional stress, may affect the main-

tenance of menstrual cycles but this does not negate the finding that a critical minimum weight appears necessary for its maintenance (Frisch & MacArthur, 1974). Frisch's hypothesis has generated much discussion from criticisms of the methodology (Trussel, 1978) to unsuccessful replication studies (Billewicz, Fellowes & Hytton, 1976). Frisch defends the hypothesis noting confirming results in animal and cadaver experiments (Frisch, 1978).

Body weight has been associated with alterations in estradiol metabolism in young women. Fishman, Boyar and Hellman (1975) reported that in women with low body weight, changes in the metabolic pathway of estradiol produces a net decrease in the estrogenic activity of the endogenous hormone. This shift in estradiol metabolism may play a significant role in anovulation resulting in secondary amenorrhea.

Vigersky and coworkers tested hypothalamic, pituitary, and endocrine function in 19 patients with secondary amenorrhea associated with simple weight loss from decreased caloric intake to evaluate the effects of weight loss on those systems. None of these patients were diagnosed as having anorexia nervosa. Weights were reported to range between 9.4 and 29.6 percent below normal, with the mean ideal body weight taken from the Metropolitan Life Insurance Company Statistical Bulletin. They concluded that patients with simple weight loss have hypothalamic dysfunction, based on the direct evidence of lack of thermoregulatory responses in heat, lack of a shivering response to hypothermia and partial diabetes insipidus. Delayed LH release after stimulation with LH releasing factor

and a lack of a diurnal variation of cortisol constitute what they termed "indirect evidence" of hypothalamic dysfunction. In general, the results in patients with simple weight loss fell between the normal controls and what has been observed in patients with anorexia nervosa (Vigersky, Anderson, Thompson & Loriaux, 1977). This study is consistent with the results obtained by Wentz, Jones & Sapp (1976) who examined patterns of gonadotropin output of patients with menstrual dysfunction. Findings indicated that the character and pattern of LH pulsatile activity varied with different forms of menstrual dysfunction. In patients with severe menstrual dysfunction the LH pulses are low to absent while in patients with less severe menstrual dysfunction, as in polycystic ovary disease, normal to increased pulsatile LH patterns were reflected. These variations in the LH pulse pattern may indicate the degree of hypothalamic dysfunction.

Yen, Rebar, Vandenberg and Judd (1973) studied the gonadotropin releasing mechanisms in a group of patients with hypogonadotropic secondary amenorrhea and otherwise normal pituitary function. In this group of eight patients, during the early follicular phase of the menstrual cycle, there were significantly decreased circulating LH and estradiol levels and the pulsatile fluctuation of LH was typically absent. The authors hypothesized that the low LH secretion and the absence of pulsatile fluctuation seen in these patients was due to a defect in the regulatory mechanism of the pulsatile component only, while the small continuous secretion of both hypothalamic GnRH and pituitary gonadotropins remained intact. The site

of the defect in LH fluctuation remained obscure.

The Effects of Exercise, Including Running, on Reproductive Hormone Levels and the Menstrual Cycle

Factors which appear to be related to the occurrence of exercise-induced oligomenorrhea and secondary amenorrhea have been identified in factor-searching and factor-relating studies completed by Feicht et al. (1978), Dale et al. (1979a), Speroff and Redwine (1980), Wentz (1980), Schwartz, Rebar and Yen (1980) Baker et al. (1981), Shangold, (1980), Carlberg, Buckman, Peake and Reidesel (1980) and Lutter and Cushman (1982). The factors identified include: age, reproductive history, particularly previous menstrual irregularity, age at menarche and nulliparity, weight loss or alteration of percentage body fat; intensity of training; and stress. The findings relative to the factors are reviewed in Table 2.

Reproductive history, including prior menstrual irregularity, previous pregnancy and age at menarche, has been evaluated in several studies, relative to the occurrence of exercise-induced menstrual irregularity. Shangold's (1980) discussion, based on an unpublished survey of 394 women marathoners, stated that prior menstrual irregularity was present in "most" of the marathoners currently experiencing secondary amenorrhea and, therefore, exercise induced amenorrhea was primarily an extension of previous menstrual patterns. In support of Shangold's hypothesis, Schwartz et al. (1980) observed that 54.5% of amenorrheic runners had prior menstrual irregularity compared with 15.5% of regularly menstruating runners. Lutter and

Table 2

Factors Related to the Onset of Oligo-Amenorrhea in Runners

Factors	Investigator(Year)[Sample Size]					
	Erdelyi(1976)	Feicht et al. (1977) [N=128]	Dale et al. (1979a) [N=90]	Schwartz et al. (1980) [N=53]	Baker et al. (1981) [N=23]	Lutter et al. (1982) [N=410]
Previous Irregularity	-			+	-	+
Ever Pregnant			+		+	
Older age at Menarche			-		+	+
Age at study					+	+
Intensity of Training	+	+	+		-	+
Weight loss/ low % body fat		-	+	+	+	+
Stress			?		?	?

Note. + = associated with oligomenorrhea or secondary amenorrhea
- = not associated with oligomenorrhea or secondary amenorrhea
? = discussed but not measured
= not reported

Cushman (1982) also reported that prior irregularity was one of the characteristics distinguishing oligo-amenorrheic athletes from eumenorrheic athletes. In contrast to those investigators' findings are those of Erdelyi (1976), Speroff and Redwine (1980) and Baker et al. (1981). Erdelyi (1976) noted that there was no increased incidence of prior menstrual irregularity in athletes and Speroff and Redwine (1980) reported that most runners who became amenorrheic had normal cycles prior to beginning a running program. Investigations of Baker et al. (1981) included only runners who had regular menstrual cycles prior to running. Of the 23 women runners studied, 39 percent previously regularly menstruating women became amenorrheic after a running program was initiated. These data do not support the "extension of prior irregularity" hypothesis as proposed by Shangold (1980).

Dale, Gerlach and Wilhite (1979a) were the first to observe that nulliparity may be associated with the development of menstrual irregularity in runners. Only 21% of previously pregnant runners compared to 51% of nulliparous runners had oligomenorrhea or secondary amenorrhea. Baker et al. (1981) reported similar results: 47% of nulliparous and 25% of parous runners experienced secondary amenorrhea since running. Dale et al. (1979a) suggested that hypothalamic maturity, demonstrated through pregnancy, decreases susceptibility to the development of menstrual irregularity. Age at menarche has been disputed as a predisposing factor to the development of exercise-induced amenorrhea. Speroff and Redwine (1980) and Dale et al. (1979a) reported a similar age

at menarche for all runners while Baker et al. (1981) and Lutter and Cushman (1982) reported a later age at menarche for oligo- or amenorrheic runners as compared to eumenorrheic runners. In addition to older age at menarche, the studies by Baker et al. (1981) and Lutter and Cushman (1982) reported at the time the study was conducted, those experiencing oligomenorrhea or secondary amenorrhea were younger. Baker et al. (1981) suggested that "younger runners, particularly those with late onset of menarche, are more prone to develop secondary amenorrhea as a consequence of running"(p. 186).

Intensity of training has been evaluated indirectly by such parameters as miles run per week, days run per week and months per year in training. Erdelyi (1976) initially noted in 1956 that during times of intense in-season training, athletes experienced amenorrhea and resumed menstruating during off-season. Feicht et al. (1978) described 128 women runners according to training regimens and incidence of amenorrhea. Six percent of women running the least (less than 20 miles per week) reported amenorrhea while 43% of those running 60 miles or more per week had amenorrhea. The amenorrheic athletes also trained more intensely for a longer number of months each year than the eumenorrheic athletes. Shangold et al. (1979) noted that with increased mileage, serum progesterone levels decreased, perhaps indicating a less functional corpus luteum with increased mileage. Dale et al. (1979a) indicated that of the runners studied, "those with the most intensive training schedules appeared to have the least number of periods." (p. 49). Lutter and Cushman (1982) reported a "statistically significant

trend toward fewer menstrual periods among runners with. . . high mileage training" (in press). However, Speroff and Redwine (1980) and Baker et al. (1981) reported similar weekly mileage for both eumenorrheic and amenorrheic runners.

The relationship between the ratio of lean body mass to body fat, low initial weight and loss of body fat, and the development of menstrual irregularities in runners have been extensively discussed. Much of the discussion has centered on the work of Frisch and MacArthur (1974) who first asserted that some critical level of body fat is necessary for the onset and maintenance of menstruation. Although agreement about the precise "critical fat level" and elucidation of exact mechanisms involved are lacking at present, it seems that body fat, particularly a decrease in body fat, is related to the development of exercise-induced amenorrhea. When compared to eumenorrheic runners, amenorrheic runners have been shown to have generally lower initial body weight for height (Dale, Gerlach & Wilhite, 1979; Speroff & Redwine, 1980; Schwartz et al., 1980), greater weight loss since the onset of training (Dale et al., 1979; Schwartz et al., 1980; Speroff & Redwine, 1980; Baker et al., 1981; Lutter & Cushman, 1982) or a lower percentage of body fat (Dale et al., 1979a; Schwartz et al., 1980; Wentz, 1980; Baker et al., 1981). Feicht et al. (1977) did report comparable mean heights and weights for both eumenorrheic and amenorrheic runners. A weight measurement, however may be misleading, since after beginning to run, the increase in muscle mass may offset the decrease in body fat, causing no gross weight change

but a substantial shift in body composition with a significant decrease in adipose tissue.

Several hypotheses have been proposed to explain the relationship between body fat and menstrual function. The excretion of estrogen is known to vary with body weight and amount of fat, and apparently, with decreased body fat estrogen pathways of metabolism are shifted towards the production of catecholestrogens (Fishman, Boyar & Hellman, 1975). Catecholestrogens may be inhibitory at the central level, suppressing cyclic menstrual function. An alternative hypothesis suggests that with a decrease in adipose tissue, a site for extragonad estrogen conversion, a hypoestrogenic milieu is created. With lowered estrogen levels, pituitary sensitivity to GnRH may be decreased, resulting in lowered gonadotropin output and decreased ovarian stimulation, compounding the problem (Wentz, 1980). As Baker (1981) stated, "alterations in the ratio of lean body mass to body fat and degrees of weight loss appear to be important factors in the onset of secondary amenorrhea in runners" (p. 693).

Stress has been mentioned by Dale et al., (1979a), Shangold (1980), Baker (1981), Lutter and Cushman (1982) and Harris (1978) as having a probable influence on the development of secondary amenorrhea in runners. Stress has been used in these reports to describe both the physical stimulus of high mileage training and the psychological response to the stimulus of competition, and finding time to run in a busy schedule, among others. None of these studies have attempted to evaluate "stress" in their runners

except to say that there may be a relationship between the stress of high mileage training and the development of secondary amenorrhea.

The alterations that occur in female reproductive hormones and menstrual cycles with exercise have been measured in a variety of studies. Acute hormonal responses to single session exercise testing have been measured by Jurkowski, Jones, Walker, Younglai and Sutton (1978), Bonen, Ling, MacIntyre, Neil, McGrail and Belcastro (1979), Keizer, Poortman and Bunnik (1980), Carlberg and associates (Carlberg, Peake, Buckman, Srivastava & Riedesel, 1980; Carlberg, Buckman & Peake, 1981; Carlberg, Peake, Buckman & Srivastava, 1981) and Shangold, Gatz and Thysen (1981). Jurkowski et al. (1978) and Bonen et al. (1979) both observed changes in selected hormones during bicycle ergometer work. In their small samples of "fairly active" regularly menstruating females measured in the follicular and luteal phases, both observed increases in estradiol levels over the exercise period. Jurkowski and associates (1978) noted that luteinizing hormone (LH) levels were unchanged with exercise while follicle-stimulating hormone (FSH) showed an increase in the follicular phase but not in the luteal phase. They concluded that exercise is a physiological stimulus to hormone elevations, with the increases related to the intensity of exercise and apparently independent of pituitary control.

Keizer et al. (1980) was concerned with the mechanisms involved with the changes in hormone levels reported by Jurkowski et al. (1978) and Bonen et al. (1979). Since the total serum hormone level is the result of production and degradation, and since Keizer and

coworkers (1980) assumed production was unlikely to be altered during a ten minute exercise test, they selected to study the degradation rate of estradiol measured as the metabolic clearance rate. Six young, healthy, physically active, regularly menstruating females, all in the follicular phase of the menstrual cycle were evaluated. In all the women, there was a consistent and sharp decrease in the metabolic clearance rate (MCR) at the end of the ten minute submaximal work effort. The 36% mean decrease in MCR may explain the mean increase of 13% and 25% in estradiol levels after exercise noted by Jurkowski et al. (1978) and Bonen et al. (1979) respectively. Keizer et al. (1980) concluded that short term physical exercise is able to induce a marked decrease in the metabolic clearance rate of estradiol in healthy young women.

The results of Jurkowski et al. (1978), Bonen et al. (1979) and indirectly Keizer et al. (1980) have not been supported by Carlberg and associates (Carlberg, Peake, Buckman & Srivastava, 1961). By studying a small group of eumenorrheic and oligo-amenorrheic college athletes, they noted that estradiol, estrone, progesterone and 17-OH-progesterone did not change significantly with exercise although there was a post-exercise increase in both testosterone and dihydrotestosterone. They suggested that the change in plasma androgen levels was not a result of decreased steroid degradation. The main differences between the two groups of studies appear to be the timing during the menstrual cycle of the samples and the type of exercise. Carlberg et al.'s (1981) subjects were in the early follicular phase of their menstrual cycles and had

completed a six mile run or two hour tennis workout, conducted at the participant's own pace. Carlberg et al.'s (1981) findings concerning the post-exercise androgen response are consistent with reports from Sutton, Coleman, Casey and Lazarus (1973) and Shangold, Gatz and Thysen (1981). Carlberg's study offers additional information about the acute hormonal response of the amenorrheic athlete, since their study included both eumenorrheic and amenorrheic athletes. They did not find significant differences in the hormonal responses of the two groups of athletes and concluded that "while plasma androgen levels rise dramatically in response to exercise in women, there was not an unusually large response in the amenorrheic athletes which may account for their menstrual dysfunction" (p. 35).

The acute response of prolactin after exercise in physically conditioned athletes has been studied with varying conclusions by Shangold et al. (1981), Brisson, Valle, DeCarufel, Deharnais and Tanaka (1980), and Carlberg, Buckman and Peake (1981). Shangold et al. (1980) and Brisson et al. (1980) both reported an increase in post-exercise prolactin levels. Four of Shangold's six subjects experienced a higher than normal level of prolactin in the post-exercise measurement. Carlberg and associates observed a post-running increase in prolactin which did not exceed the range of normal. Further, Carlberg, Buckman and Peake (1981) did not observe differences in the responses of eumenorrheic and oligo-amenorrheic athletes, and suggested that "prolactin may not play a role in the development of athletic amenorrhea" (p. 7).

The acute response of the gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), have been evaluated in physically active females by Jurkowski et al. (1978), Schwartz, Rebar and Yen (1980), Demers, Harrison, Halbert & Santen (1981), Shangold et al. (1981) and Carlberg, Peake, Buckman, Srivastava & Riedesel (1981). The results reported are inconsistent, perhaps due to the differing study protocols used. A summary of the results reported are located in Table 3.

Non-acute hormone studies have included those completed by Dale et al. (1979a), Shangold et al. (1979), MacArthur, Bullen, Beitins, Pagona, Bagner, Klibanski (1980), Wentz (1980), Webb (1981) and Baker et al. (1981). Dale and associates (1979a) provided the first non-acute hormone data on women runners. The hormone profile of the amenorrheic runner they documented has generally been supported, as studies since published present similar results. Dale et al.'s (1979a) study of 20 runners showed that ovulatory runners had normal, cyclically fluctuating levels of estradiol, testosterone, progesterone, FSH and LH while anovulatory runners had suppressed, non-cyclic values. Webb (1981), who studied 13 runners and Baker et al. (1981) whose study involved 23 runners, both reported similar depressed and non-cyclic hormone values for amenorrheic runners as compared to regularly menstruating runners. Additional confirmation of the data presented by Dale et al.(1979a) was provided by Wentz (1980) and MacArthur et al. (1980) who both reported low baseline levels of LH in amenorrheic runners. Shangold et al.'s 1979 study provided information about the development

Table 3

Acute Response of Gonadotropins to Exercise in Females

Investigator, Year	FSH	LH
Jurkowski et al., 1978	Increased in mid-follicular phase only.	No effect
Schwartz et al. , 1980		
Amenorrheic runners	No effect	Elevated
Eumenorrheic runners	No effect	No effect
Shangold et al., 1981	No effect	No effect
Carlberg et al., 1981		
Amenorrheic runners	Not reported	Decreased
Eumenorrheic runners	Not reported	No effect
Demers et al., 1981	Decreased	Decreased

of decreased progesterone in runners. They noted a decrease in progesterone levels in cycles during which mileage was increased. Prolactin levels, also measured by Dale et al. (1979a), were lower in runners, a finding supported by the work of Baker et al. (1981). In contrast, Wentz (1980) reported a normal prolactin level in an amenorrheic runner, and Carlberg, Buckman and Peake (1981) documented normal baseline prolactin levels in five eumenorrheic and five amenorrheic college athletes.

Hypotheses resulting from these studies have included those of Dale, Gerlach and Wilhite (1979) who suggested that using the serum hormone measurements, it is "possible to define the probable site of dysfunction in the hypothalamic-pituitary-ovarian axis" (p. 51). MacArthur et al. (1980) stated that the normal to hyperresponsiveness of LH and FSH response to GnRH stimulation support the hypothalamus as the site of dysfunction. It is difficult to identify a particular "site of dysfunction" in a system as complexly interdependent as is the regulatory system for the female reproductive cycle, particularly when alterations appear to occur at all three of the primary regulatory organs.

Other responses to physical exercise not unique to the female have been documented and include increased cardiovascular endurance as measured by increased $\dot{V}O_2$ maximum (Yaeger & Brynteson, 1970; Kilbom, 1971; Drinkwater, 1973; Pollock, 1973; Wilmore & Brown, 1974; Fringer & Stull, 1974; Cunningham & Hill, 1975; Kollis, Bartlett, Oja & Shearburn, 1977; Eddy, Sparks & Adelizi, 1977; Lamb, 1978; Dale et al., 1979b); decreased percent body fat (Moody, Kollias,

& Buskirk, 1969; Mayhew & Gross, 1974; Wilmore, 1974; Dale et al., 1979b, Schwartz et al., 1980, Wentz, 1980; Lutter & Cushman, 1982); and increased serum high-density lipoprotein cholesterol (Drinkwater, 1973; Wilmore & Brown, 1974; Wood, Haskell, Stern, Lewis & Perry, 1977; Lamb, 1978; Dale et al., 1979b; Gordon, Kannel & Castelli, 1981). Although a number of studies have been completed assessing the effects of exercise on serum lipids they have been performed primarily on men (Taylor, 1959; Hollozy, Skinner, Toro & Cureton, 1964; Campbell & Lumbsden, 1967; Taylor, Anderson & Keys, 1967, Hoffman & Goss, 1967; Mann, Garrett, Farhi, Murray & Billings, 1969; Altekruse & Wilmore, 1973; Lopez, Vial, Balart & Arroyave, 1974; Penny, 1975; Wood, Haskell & Klein, 1976; Enger, Herbjorsen, Erkssen & Fretland, 1977; Roundy, Fisher & Anderson, 1978; Adner & Castelli, 1981; Weltman, Matter & Stamford, 1980).

Research Questions

1. In a group of women runners, are there significant relationships between the number of menstrual periods per year and factors discussed by other investigators, including:
    a. age at the time of the study
    b. age at menarche
    c. prior menstrual irregularity
    d. previous pregnancy
    e. percent body fat, body weight or weight loss
    f. training intensity.
2. In a group of women runners, are there significant rela-

tionships between the number of menstrual periods per year and factors not previously investigated, including:

a. Nutritional factors

b. General life stress

c. Running associated stress.

3. In a group of women runners, are there significant relationships among serum lipid levels, percent body fat, dietary cholesterol, and serum estrogen levels?

CHAPTER III

METHODOLOGY

Design

This was a nonexperimental correlation study. Menstrual and running history questionnaires and the Schedule of Recent Events questionnaire were completed by each participant. One time observations of physical conditioning as estimated by oxygen uptake during submaximal stress testing, percent body fat as estimated by skinfold thickness measurement, and serum cholesterol, lipoproteins, triglycerides and ovarian hormones as measured by appropriate laboratory procedures were made on normal, sexually mature, non-pregnant, non-smoking Caucasian women runners aged 18-37. The relationships among variables hypothesized to be related to menstrual irregularity were then evaluated using multiple correlation and regression techniques.

Definitions

Normal

The term normal indicates that subjects did not have any known systemic or reproductive system disease or any other physical or psychological impairments that might have affected their participation in the study.

Oligomenorrhea

Oligomenorrhea refers to the irregular, infrequent (less than nine but greater than four per year) occurrence of menstruation after the establishment of regular menstrual cycles.

Regular Menstrual Cycles

The recurrence of menstruation on a regular basis occurring at least nine times per year is defined as a regular menstrual cycle.

Secondary Amenorrhea

The decrease in occurrence of menstruation three or fewer times per year after regular menstrual cycles had been established.

Sexually Mature

The time interval between establishment of a regular menstrual pattern and the onset of symptoms of menopause.

Sample

The sample consisted of women who met the following criteria for inclusion in the study:

1. between the ages of 18 and 38;
2. not on birth control pills or other steroid hormone medications for three months prior to participation in this study;
3. no systemic or reproductive system disease which would affect participation in the study;
4. not pregnant or lactating at the time of participation in this study;

5. had run for the past year, and currently ran 30 miles/ week or more, and

6. non-cigarette smokers.

Data reported here excludes some study participants. One hundred and twenty women were involved in the study: 30 were non-runners, eumenorrheic controls interested in beginning an exercise program and 12 were post menopausal women.

Two black runners who met all criteria for inclusion participated in the study but were excluded from the group data analysis due to the small number of black participants and the possible introduction of additional unexplained variation in the results. Six other runners met all criteria for inclusion except for current birth control pill use and were also excluded from data analysis. Data on 70 runners are reported here.

Sampling

The self-selected sample was obtained in Atlanta, Georgia by individually contacting members of local running clubs and advertising the study through the local running newsletters and stores selling running equipment. The researcher explained the purpose of the study and what participation involved to all contacts. Those who met the inclusion criteria and verbally agreed to participate were mailed a study packet. The packet contained a cover letter, an instruction sheet, a copy of the Informed Consent form, questionnaires, maps and a diet diary form provided by the Emory University Center for Nutrition and Dental Health. Subjects were asked to contact the researcher at the beginning of their next men-

strual cycle bleeding phase to make the appropriate blood sampling appointments. Appointments for submaximal stress testing and body fat measurements were set at a time convenient for the participants. Not all runners who received packets in the mail participated due to injuries or reduced weekly mileage experienced after receiving the packet (n=6), time constraints experienced by the subjects (n=2) and unexpected pregnancy (n=1).

Blood Sample Appointments. Each participant was initially scheduled for two blood sampling appointments; the first on the 11-14th day of her menstrual cycle, and the second ten days later on the 21-24th day of her cycle. Participants were asked not to drink alcohol or take vitamins the evening before their scheduled appointments to avoid artificial alterations in serum cholesterol levels. Participants were also asked not to eat or exercise the morning prior to their appointments. Appointments were generally scheduled between 8:00 a.m. and 9:00 a.m.

Standard venipuncture technique was used to draw approximately 35 ml of blood from a peripheral site. Unexpired serum separater tubes were used to collect samples. After clot retraction, samples were centrifuged for eight minutes at 3000 rpm and the unhemolyzed serum was transferred to previously unused storage vials. All samples were kept frozen at -80°C until laboratory testing was performed. A batch approach for all tests except progesterone was selected to limit the number of times each test was performed, minimizing the interassay variation between results. The progesterone assay was performed at weekly intervals

on all samples collected during the previous seven days. If a participant had reported regular cycles, but had a non-ovulatory progesterone level (3 ng/ml) an additional appointment was made in an attempt to obtain an ovulatory sample. If a third appointment was scheduled, it was conducted under the same conditions as the first two appointments.

Submaximal treadmill stress testing. Submaximal stress testing was done at Georgia State University (GSU) by a GSU exercise physiology graduate assistant. The GSU protocol for submaximal stress testing on a motor driven treadmill developed by Dr. G. Rankin Cooter based on the American College of Sports Medicine's Guidelines for Graded Exercise Testing and Exercise Prescription (1980) was used for all tests. This protocol, designed to increase the estimated oxygen uptake by 10 $ml \cdot kg^{-1} \cdot min^{-1}$ at the end of each stage, used grades and speeds as indicated in Table 4. No one in the study exceeded stage 7. Using a CM5 lead (Morehouse, 1972) with telemetry, heart rate and electrocardiogram were monitored using the following instruments: Biotachometer (BT 1200), Biotelemetry Receiver FM 100, Digital Display DD350, Physiograph Desk Model DMP-4A, all distributed by Narco Biosystems, Inc., Houston, Texas. Recordings were made at rest, after a 30 second hyperventilation test interval, on the treadmill at one minute intervals, and for a five minute posttest recovery period. One subject had infrequent ventricular ectopic beats at rest and was not tested at that time. Subsequently, she was evaluated on a maximal treadmill stress test by a cardiologist without incident. Four subjects had ventricular ectopic beats

Table 4

Treadmill Testing Protocol: George State University's Human Performance Laboratory

Stage	Minute	MPH	Grade
1	1-2	3.0	3%
2	3-5	4.0	5%
3	6-8	4.0	10%
4	9-11	5.0	10%
5	12-14	6.0	10%
6	15-17	7.0	10%
7	18-20	7.0	15%
8	21-23	7.5	15%

during the five minute posttest recovery period, but none exceeded five ectopic beats per minute, and all were asymptomatic with normal blood pressure readings.

The maximum oxygen uptake was estimated from the time on the treadmill, using the guidelines of the American College of Sports Medicine (See Table 5).

Cooper (1978) indicates that the $\dot{V}O_2$ max results may be grouped by physical fitness categories as reflected in Table 6. Differentiation by age was based on "the natural decrease in maximal working capacity as a person grows older." (p. 21). The tables also differ for men and women as well, according to statistically demonstrable difference in physiological variables, such as heart and lung size, between men and women.

The use of the $\dot{V}O_2$ max results in this study is somewhat limited by the estimation of $\dot{V}O_2$ max from the time on the treadmill as opposed to direct measurement of oxygen consumption using a maximal testing protocol. A submaximal testing protocol was selected because it provides a reasonable estimate of the $\dot{V}O_2$ max with a minimum of discomfort and time involvement on the part of the subjects. Variables which affect the estimation of $\dot{V}O_2$ max from time on the treadmill and which do not affect a direct measure of $\dot{V}O_2$ max are primarily those which affect heart rate: Stress and the ingestion of drugs or foods containing caffeine are variables which artificially elevate the heart rate, and could cause a premature end of the testing. Participants were cautioned about the ingestion of caffeine containing foods

Table 5

Estimated Maximal Oxygen Uptake by Time on Treadmill

Stages	Minutes Completed on Treadmill	Estimated $\dot{V}O_2$ Max ($ml \cdot kg^{-1} \cdot min^{-1}$)
1	1	9.1
	2	18.2
2	3	21.0
	4	24.3
	5	27.4
3	6	31.0
	7	34.8
	8	38.6
4	9	41.9
	10	45.1
	11	48.3
5	12	51.3
	13	54.3
	14	57.4
6	15	60.4
	16	63.4
	17	66.4
7	18	69.6
	19	72.8

Table 6

Cooper's Aerobics Fitness Classifications for Women

Fitness Category	$\dot{V}O_2$ max ($ml \cdot kg^{-1} \cdot min^{-1}$)		
	13-19 years	20-29 years	30-39 years
Very poor	< 25.0	< 23.6	< 22.8
Poor	25.0 - 30.9	23.6 - 28.9	22.8 - 26.9
Fair	31.0 - 34.9	29.0 - 32.9	27.0 - 31.4
Good	35.0 - 38.9	33.0 - 36.9	31.5 - 35.6
Excellent	39.0 - 41.9	37.0 - 40.9	35.7 - 40.0
Superior	> 42.0	> 41.0	> 40.1

Note. Adapted from Cooper, 1978.

especially coffee. It appeared that anxiety about the testing was present in some subjects although after beginning to exercise, the heart rate initially decreased in those subjects. In general, the $\dot{V}O_2$ max was probably slightly underestimated in these subjects.

Body fat measurements. Measurement of subcutaneous skinfold fat with constant pressure Harpenden Skinfold Calipers was used to estimate body density from which the percent of body fat was calculated. A vertical skinfold over the iliac crest in the midaxillary line and a vertical skinfold on the back of the arm taken halfway between the acromion and olecranon processes with the elbow extended were measured. All measurements were made on the right side of the body with the subject standing. The measurements were taken by the researcher three times with an average of the measures recorded. The formulas for calculation of body density developed by Sloan, Burt and Blythe (1962) and body fat as developed by Brozek, Grande, Anderson and Keys (1963) were used to estimate percent body fat. Height and weight were also recorded. Ponderal index was calculated from the height and weight using the following formula

$$\frac{\text{Height in Inches}}{\sqrt[3]{\text{Weight in pounds}}}$$

(Ryan & Allman, 1974).

Precautions were taken to insure that all measurements were conducted in the same manner using the same equipment and the same

researcher. Skinfold thicknesses to estimate body density minimized the discomfort and time involvement of participants. The precision of the body fat estaimte using skinfold thicknesses is limited by technical measurement error and by use of a formula to derive the percent body fat. The body density formula used here was developed by Sloan et al. (1962) based on measurements of a North American Caucasian female population, aged 17-24. The age of participants in this study ranged from 18-36 years. Flint, Drinkwater, Wells and Horvath (1977) studied the application of a variety of formulas used in estimating body fat and stated that those more accurate in predicting body fat in young women were not as useful in predicting body fat in women over 35 years of age. Since only two women were over 35 in this study, the report of Flint et al. (1977) supports the use of the formula of Sloan et al. (1962) in this sample although the formula was applied to an age population other than the one from which it was derived.

Nutritional assessment. Each participant was asked to complete the Nutran diet diary (Emory University Center for Nutrition and Dental Health) two days prior to each blood sampling, for a total of four days. Participants were asked to eat normally, but record in detail the foods consumed, listing brand names, recipes for unusual dishes and identification of restaurants to facilitate making as accurate an estimate as possible of what was eaten. The information recorded by subjects was translated into computer codes by registered dieticians in the Center for Nutrition and Dental

Health, Emory University, and analyzed by the central computing facility at Emory University, Atlanta, Georgia.

A nutritional assessment score (NAS) was calculated for each participant based on the intake of fifteen nutrients, including calories, protein, calcium, phosphorus, magnesium, iron, zinc, Vitamins A,E,C, and B-vitamins thiamine, riboflavin, niacin, folic acid and B_{12}. The score was based on the assumption that the recommended daily allowance (RDA) is a sufficient intake of each nutrient and that any intake above the RDA is equivalent to 100% of the RDA. It was also assumed that since the nutrients have interactive and synergistic effects, they are of equal importance to the body and therefore, were not weighted. The NAS was computed by averaging the daily deficit percentage from 100. A score of 90 would then indicate that, on the average, 90% of the RDA of vitamins and minerals was being consumed or an average 10% deficit in intake of the RDA of vitamins and minerals was present (Kreitzman, 1981).

The estimation of nutritional intake by a diet diary is limited by the recall of the participant as well as the detail with which the diary is kept. A participant's perception of the amount or weight of food ingested also contributes to the variability of the assessment.

History and SRE Questionnaires. At either the first blood sampling appointment or the submaximal stress testing, whichever occurred first, the participants signed the informed consent (See Appendix B) after all questions were answered. At the first contact, participants brought with them their completed Schedule

of Recent Experiences (SRE) and menstrual and running history questionnaires which had been previously mailed. Any questions the participants had about the questionnaires were clarified and any incomplete questions on the history questionnaire were discussed with the participant and completed.

The Schedule of Recent Experiences (Appendix C) was used with permission of its developer, Thomas H. Holmes, University of Washington Medical School, Seattle, Washington. The SRE evolved from the work of Meyer's "life chart" which documented biologic, psychologic and sociologic processes in relation to health and disease. The current SRE questionnaire sought information about the occurrence of 42 life events, including the major areas of personal, family and peer relations, economics, education, occupation, religion, recreation and health. Participants were asked to record the number of times each life event occurred during the past year. Each item had a weighted score associated with it; the item score was multiplied by the number of times each event occurred in the past year. Four or more occurrences were scored as four. The item scores were then added for a total "life change units" score. Holmes and others (Holmes & Masuda, 1973; Holmes & Holmes, 1974) have stated that the higher the score, the greater the likelihood a health change will occur. Holmes has indicated that a score of less than 150 life change units is associated with a 30% chance of experiencing an illness; 150-300 is associated with a 50% likelihood of becoming ill; a score greater than 300 is associated with an 80% risk of becoming ill (Amundson, Holmes & Hart, 1981).

The questionnaire was selected for use in this study because it was developed from a healthy population and does not focus on a certain aspect of experience, as do many other "stress" questionnaires (Miller, 1981). Although Holmes and Holmes (1974) do not associate "stress" with this questionnaire, it does assess life change events. Since these events are a stimulus for adaptation or other change and are related to the development of illness, it would appear that the questionnaire evaluates the presence of "stress," if defining stress as a stimulus instead of a response. The controversy surrounding this questionnaire has been the assignment of points to each life event, based on the responses of the test populations involved in the development of the SRE. This limits the findings associated with this questionnaire, since not all participants might evaluate the same life events in the same way.

The history questionnaire was based on a similar questionnaire developed for previous studies of Dale et al. (Dale et al., 1979a,b) and included questions about both reproductive and running histories. It was modified by the researcher to obtain information about three general time intervals: from menarche to 18 years; from 18 to whenever the subject began running; and within the time interval since running, particularly the previous year (Appendix C).

The menstrual irregularity score (MIS) was calculated for two time intervals; from menarche until 18 years of age (MIS I) and from 18 years until beginning to run (MIS II). The score was

calculated from three questions on the menstrual history questionnaire regarding the frequency of occurrence of menstrual cycles, the regularity of occurrence and the length of the bleeding phase of the menstrual cycle (4,5,6 History Questionnaire in Appendix C). Responses were scaled and assigned a point value. One point was given for very regular or normal, two points for slightly irregular or slightly outside the range of normal, and three points for very irregular or grossly abnormal. The scores for the three questions were summed for the MIS. A score of three indicated regular, normal cycles, while a score of nine would indicate an irregular, abnormal running history.

The running stress score was calculated from four questions on the running history questionnaire concerning the participants' perceptions of the stress of running (34, 35, 36, 37, History Questionnaire in Appendix C). These questions included perceptions of psychological stress as well as of physical stress. The responses were scaled from no stress to very stressful and assigned points from one to four. The points assigned to the responses to the four questions were then summed to arrive at the running stress score. A score of four indicated that the participant perceived running as non-stressful, while a score of 16 would indicate that running was a very stressful experience to that participant.

A running stress score is very limited in application. A systematic scale development should be done to thoroughly evaluate all aspects of stress associated with running. The questions used here are preliminary to a more exhaustive investigation of the

stress of running and only gave limited information about the runners' perceptions of the stress of running.

Laboratory Analysis. Each participant had a mid-luteal blood sample analyzed for progesterone. All other laboratory assessments were performed simultaneously on both a late-follicular and mid-luteal sample, for those subjects experiencing regular menstrual cycles. For anovulatory subjects, two samples obtained at a ten day interval were also analyzed simultaneously. These assessments included total serum cholesterol, serum triglyceride, HDL cholesterol, LDL cholesterol, estradiol and testosterone.

Triglycerides were determined in duplicate with an Instrumentation Laboratories (IL) Test Triglycerides kit, (1979) used with an IL Multistat III Micro Centrifugal Analyzer (MCA). This test kit is based on a modification of the Bucolo and David method (1973). Total cholesterol levels were determined in duplicate with an IL Test Cholesterol kit, also used with the IL Multistat III MCA. The kit uses a modification of the Allain, Poon, Chan, Richmond and Fur (1974) method. Pre-exercise, fasting serum samples which had been frozen for no longer than two months at -80° C and which were collected according to the protocol previously described were used for triglyceride and total cholesterol analysis, as well as lipoprotein determinations.

The method used for determination of HDL cholesterol was based on isoelectric polyanionic precipitation of VLDL and LDL developed by Burnstein (Burnstein, 1970) using a phosphotungstate reagant (Rutkowski, 1979). The LDL cholesterol values were

estimated from the total cholesterol, HDLC and triglycerides values, using the following formula:

$$\text{Total Cholesterol} - \left(\frac{\text{Triglycerides}}{5} + \text{HDLC} \right) = \text{LDLC}$$

(Rutkowski, 1979).

The hormone assays were performed in duplicate using radioimmunoassay techniques by Wright, Collins, Mussey and Preedy (1978) and Cameron and Scarisbrick (1973), also using pre-exercise fasting serum samples frozen at -20° C for no longer than four months.

Human Subjects Considerations

This study was approved as a minimal risk study prior to its initiation by the Review of Research with Human Subjects (Medical Area) Committees, at both the University of Utah, Salt Lake City, Utah and Emory University School of Medicine, Atlanta, Georgia. All subjects signed an Informed Consent Form prior to participation, were free to ask questions or withdraw from the study at any time and did not receive financial compensation for participating in the study.

All data were analyzed using either the Statistical Package for the Social Sciences (SPSS) subprograms for frequency distributions (SPSS), Pearson product-moment correlation coefficients and multiple regression or the Biomedical Data Processing (BMDP) subprogram for best possible subsets regression. A significance level

of .10 is reported based on the small sample size and the non-experimental design of the study (Labovitz, 1968).

CHAPTER IV

RESULTS

The data are presented by groups based on the number of menstrual cycles in the past year. Pearson product-moment correlation coefficients represent the zero-order correlations between the measured variables and the number of menstrual cycles in the past year. The majority of runners in this sample, 77% were eumenorrheic, while 10% were oligomenorrheic and 13% were amenorrheic.

Variables Associated with Number of Menstrual Cycles Per Year

Demographic Variables

The mean age of participants is similar to those in previous studies (Dale et al., 1979a; Baker et al., 1981; Lutter & Cushman, 1982). The mean age of eumenorrheic and amenorrheic groups are generally the same as those reported by Baker et al. (1981) and Lutter and Cushman (1982). Age at the time of study and the related number of years of education were significantly correlated with the number of menstrual cycles in the past year. Other demographic data are summarized in Table 7.

Reproductive History

Menstrual history from menarche until 18 years old and from

Table 7

Summary of Demographic Descriptors

Descriptors	All Runners (n=70)	Menstrual Cycles in Past Year: 9+ (n=54)	8-4 (n=7)	3-0 (n=9)	r
	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Mean age at time of study	29.6 (4.7)	30.5 (4.3)	27.7 (3.9)	25.2 (5.3)	.40***
Mean years education	15.9 (2.4)	16.2 (2.3)	15.7 (2.9)	14.7 (2.6)	.20*
Occupation					
Outside home	75%	78%	72%	56%	
Homemaker	16%	19%	14%	--	
Student	9%	3%	14%	44%	

Note. r = correlation coefficient with number of menstrual cycles in past year
* = significant at .10 $\geq$ p >.05
** = significant at .05 $\geq$ p >.01
*** = significant at .01 $\geq$ p >.001

18 years of age until beginning to run is included in Table 8. The mean age of menarche of 12.9 years for all runners is slightly above the current national average of 12.5 years; but there was no statistically significant relationship between age at menarche and the number of menstrual cycles in the past year, similar to the findings of Dale et al. (1979a), but in contrast to the reports of Baker et al. (1981) and Lutter and Cushman (1982). The menstrual irregularity score calculated for all participants was slightly higher in the menarche to 18 years old interval than in the 18 years until running interval reflecting a higher degree of menstrual irregularity during adolescence. None of the amenorrheic runners reported menstrual irregularity in the time interval from 18 until beginning to run, consistent with the findings of Baker et al. (1981) and Erdelyi (1976). Previous pregnancy and prior birth control pill use are also included in Table 8; neither factor had a statistically significant relationship to the number of menstrual cycles in the past year. Dale et al. (1979a) as well as Baker et al. (1981) did report an association between nulliparity and amenorrhea in runners.

Since beginning to run, 45% of all runners reported a decrease in frequency of menstruation; 47% reported a decrease in discomfort and 65% reported a decrease in blood flow associated with menstruation. Even of the eumenorrheic runners, 32% reported a decrease in frequency of menstruation since beginning to run, 39% reported a decrease in discomfort and 58% reported a decrease in blood flow with menstruation. Eumenorrheic runners reported an average of 11

Table 8

Menstrual History Prior to Running

Variable	All Runners (n=70)	Menstrual Cycles in Past Year 9+ (n=54)	8-4 (n=7)	3-0 (n=9)	
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	r
Age at menarche	12.9 (1.3)	12.7 (1.3)	13.2 (1.3)	13.1 (1.1)	-.15
Menstrual irregularity menarche to age 18 (Yes)	18%	15%	43%	11%	
Menstrual irregularity score (I)	4.5 (2.0)	4.3 (2.0)	6.0 (2.8)	3.9 (1.3)	.07
Menstrual irregularity 18 until running (Yes)	8%	7%	33%	0%	
Menstrual irregularity score (II)	3.8 (1.4)	3.7 (1.2)	5.2 (2.9)	3.3 (.5)	.12
Pregnant (yes)	42%	36%	66%	29%	.06
Birth control pill use (yes)	77%	73%	100%	57%	.10
Months on birth control pills	45.3(31.2)	42.7 (29.6)	69.7 (35.8)	34.8 (30.8)	.08

Note. r = correlation coefficient with number of menstrual cycles in past year;
* = significant at .10 $\geq$ p $>$ .05 ** significant at .05 $\geq$ p $>$ .01; ***significant at .01 $\geq$ p $>$ .001.

menstrual cycles in the past year; oligomenorrheic runners reported an average of five; while amenorrheic runners reported an average of one menstrual cycle in the past year. Since beginning to run, six currently eumenorrheic and one currently oligomenorrheic participants had been pregnant. The outcomes of pregnancy included six miscarriages or abortions and one full-term delivery without complications (See Table 9).

Running History

The running history of participants in this study was similar to those who participated in the Dale et al. (1979a) as well as Baker et al. (1981) studies. In these studies, weekly mileage was generally 40 miles a week, with running taking place just over five days per week, for an average of 49 weeks per year. Weekly mileage was similar for all groups in this study, while there were inverse correlations between days per week running and weeks per year running with number of menstrual cycles in the past year. Amenorrheic runners generally reported a faster training time (minutes per mile), a variable also significantly related to the number of menstrual cycles in the past year (See Table 10).

Stress Testing

Submaximal treadmill testing indicated that particpants had a mean estimated $\dot{V}O_2$ max of 40 $ml \cdot kg^{-1} \cdot min^{-1}$ which places them, on the average, in Cooper's excellent fitness category (See Table 6). The estimated $\dot{V}O_2$ max was greater in the faster and longer training amenorrheic group, and showed an inverse relationship with the

Table 9

Menstrual History Since Beginning to Run

Variable	All Runners (N=70)	Menstrual Cycles in Past Year		
		9+ (n=54)	8-4 (n=7)	3-0 (n=9)
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)
Frequency of Cycles				
Increase	8%	10%	--	--
No Change	45%	58%	--	--
Decrease	47%	32%	100%	100%
Discomfort with Cycles				
Increase	8%	7%	29%	--
No change	45%	54%	29%	--
Decrease	47%	39%	42%	100%
Flow with Cycles				
Increase	7%	8%	14%	--
No Change	28%	34%	--	--
Decrease	65%	58%	86%	100%
Pregnant				
Yes	9%	10%	14%	--
No	91%	90%	86%	100%
Number Cycles in Past Year	9.6(3.9)	11.3(1.7)	4.6(0.8)	1.0(1.5)

Table 10

Summary of Running History

	All Runners (N=70)	Menstrual Cycles in Past Year			
		9+ (n=54)	4-8 (n=7)	0-3 (n=9)	r
	$\bar{X}$ (S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Months running	43.8(27.9)	45.6(29.6)	40.2(26.2)	34.0(13.4)	.15
Weekly mileage	40.5(10.5)	40.0(10.2)	42.8(15.0)	42.2(9.7)	-.06
Average training time/mile (secs.)	492.8(36.6)	499.8(30.3)	484.0(61.1)	453.0(27.8)	.37***
Average days per week running	5.5(.6)	5.4(.6)	5.4(.5)	5.9(.3)	-.24**
Average weeks/year running	47.0(3.2)	47.0(3.1)	47.0(4.9)	49.4(2.2)	-.27**

Note. r = correlation coefficient with number of menstrual cycles in past year
* = significant at $.10 \geq p > .05$; ** significant at $.05 \geq p > .01$ *** significant at $.01 \geq p > .001$.

number of menstrual cycles in the past year. Resting heart rate and blood pressure were similar for all groups and were consistent with those reported for physically conditioned females (Dale et al., 1979b; Wood et al., 1977; Drinkwater, 1973) (See Table 11).

Studies have shown that training intensity is the best predictor of $\dot{V}O_2$ max (American College of Sports Medicine, 1979). It was assumed that training time per mile was an indicator of intensity of exercise, while duration and frequency of exercise were more accurately estimated by variables such as months running, miles run per week and number of days per week per year running. To evaluate this assumption, a correlation matrix, including these variables was examined (See Table 12). To further investigate the best predictor of $\dot{V}O_2$ max in this study, a multiple stepwise regression analysis was performed. Training time per mile explained 25% of the variation in $\dot{V}O_2$ max, with the other variables held constant, while age explained 12% of the variation. The other variables made small contributions. The total corrected variation explained by all variables was 41%. This analysis supported the assumption that training time per mile contributes more to $\dot{V}O_2$ max than do frequency and duration of training and therefore, training time per mile is probably a good indicator of intensity of exercise.

Body Composition

In examining the body composition assessment, there were significant correlations between the number of menstrual cycles in the past year and body weight, percent body fat, and ponderal

Table 11

Submaximal Treadmill Test Results

Variables	All Runners (N=70)	Menstrual Cycles in Past Year 9+ (n=54)	4-8 (n=7)	0-3 (n=9)	r
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Seconds on treadmill	532.0(154.7)	510.0(152.6)	549.0(140.4)	660.0(123.7)	-.27**
Estimated $\dot{V}O_2$ max	40.0(8.6)	39.8(8.6)	42.1(7.5)	48.2(6.4)	-.27**
Resting heart rate	58.0(9.2)	59.0(8.5)	60.0(12.2)	50.0(8.3)	.28**
Resting blood pressure	108/69 (9.2/7.1)	109/70 (9.6/6.4)	104/69 (4.5/8.2)	103/63 (8.0/8.9)	

Note. r = correlation coefficient with number of menstrual cycles in past year; * = significant at .10 $\geq$ p $>$.05; **significant at .05 $\geq$ p $>$.01; ***significant at .01 $\geq$ p $>$ .001

Table 12

Intercorrelations Between $\dot{V}O_2$ Max and Running History Variables

		1	2	3	4	5	6	7
1.	$\dot{V}O_2$ max		-.06	-.50***	.23*	.04	.24**	-.49***
2.	Months running			-.01	-.08	-.03	.01	.09
3.	Training time per mile				-.16	-.32***	-.37***	.34***
4.	Days per week running					.20*	-.16	-.20*
5.	Weeks/year running						-.32***	-.20*
6.	Weekly mileage							.10
7.	Age							

Note. r = correlation coefficient with number of menstrual cycles in past year;
* = significant at $.10 \geq p > .05$
** = significant at $.05 \geq p > .01$
*** = significant at $.01 \geq p > .001$

index, consistent with the findings of previous studies (Dale et al., 1979a; Schwartz et al., 1980; Wentz, 1980; Baker et al., 1981; Lutter & Cushman, 1982). Weight loss was not significantly correlated with the number of menstrual cycles in the past year, differing from the results of Speroff and Redwine (1980) and Wentz (1980) (See Table 13).

Nutritional Assessment

The results of selected aspects of the nutritional assessment, including the Nutritional Assessment Score and daily average intake of calories, carbohydrates, fats, protein and cholesterol, have been summarized (See Table 14). The overall mean showed an intake of carbohydrates and fats within the RDA, protein intake above recommended levels and caloric and cholesterol intake well below the RDA. Approximately one third of the participants reported being on a weight reduction diet. Dale and Goldberg (1981) previously used the Nutran diet diary and the Emory University Center for Nutrition and Dental Health nutritional analysis services in a similar group by age, weight and weekly running mileage. A comparison of the group means of these two investigations indicates that the group of runners in this study reported a lower intake of the nutrients examined than those runners studied by Dale and Goldberg (1981) (See Table 15). Dale and Goldberg (1981) did not specifically report the nutritional intake of the amenorrheic athletes. In this study, the amenorrheic group had a noticeably reduced caloric, fat and cholesterol consumption. All of the nutritional variables in

Table 13

Mean Body Composition Assessment Results

Variable	All Runners (N=70)	Menstrual Cycles in Past Year			r
		9+ (n=54)	4-8 (n=7)	0-3 (n=9)	
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Height (cm)	163.5(5.5)	163.2(5.4)	166.2(4.5)	163.6(6.9)	.01
Weight (kg)	54.5(5.9)	55.0(5.4)	55.7(7.2)	49.9(6.7)	.29**
Body fat (%)	18.1(2.5)	18.4(2.6)	17.9(2.4)	16.4(1.6)	.26**
Weight change in past year (kg)	-1.0(3.5)	-1.3(3.0)	-3.7(6.8)	-1.6(3.4)	.11
Ponderal index	13.1(.3)	13.0(.3)	13.2(.5)	13.5(.5)	-.32***

Note. r = correlation coefficient with number of menstrual cycles in past year

* = significant at $.10 \geq p > .05$
** = significant at $.05 \geq p > .01$
*** = significant at $.01 \geq p > .001$

Table 14

Mean Nutritional Assessment Results

Variable	All Runners (N=70)	Menstrual Cycles in Past Year: 9+ (n=54)	4-8 (n=7)	0-3 (n=9)	r
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Nutritional Assessment Score	83.0(9.9)	84.0(9.7)	80.0(6.9)	81.0(12.6)	.24**
Average daily calories	1732.0(476.6)	1769.0(482.5)	1806.0(303.0)	1450.0(495.2)	.39***
Average daily carbohydrates (g) (RDA=100-281 g)	203.0(58.6)	205.0(60.8)	216.0(56.3)	181.0(44.8)	.24**
Average daily fats (g) (RDA = < 78g)	75.0 (29.9	77.0(29.8)	81.0(28.0)	59.0(29.7)	.40***
Average daily protein (g) (RDA = 44 g)	66.0(20.5)	69.0(20.6)	56.0(8.8)	55.0(22.0)	.39***
Average daily cholesterol (mg)(RDA= < 500 mg)	381.0(202.8)	414.0(207.6)	327.0(141.1)	226.0(130.9)	.46***

Note. r = correlation coefficient with number of menstrual cycles
* = significant at .10 $\geq$ p > .05; ** significant at .05 $\geq$ p > .01; *** significant at .01 $\geq$ p > .001.

Table 15

A Comparison of Nutrient Intake of Women Runners

Nutritional Variables	Dale & Goldberg (1981)	Present Study (1982)
Calories	2135	1732
Carbohydrates (g)	224	203
Fats (g)	88	75
Protein (g)	74	66
Cholesterol (mg)	452	381

Table 14 have significant correlations with the number of menstrual cycles in the past year.

Laboratory Analyses

Results of the laboratory analyses of serum are reported by late follicular and mid-luteal values (See Tables 16 and 17). All laboratory analysis results, except for the mean estradiol levels in the amenorrheic group, are within the ranges of normal. The estradiol values of the amenorrheic group are similar to those reported by Dale et al. (1979a) and Baker et al. (1981). The total cholesterol and HDL cholesterol values are consistent with those reported by Dale et al. (1979b) and Wood et al. (1977) for the physically conditioned females. The mean total cholesterol/HDL ratio indicates that all groups have below average risk for developing coronary heart disease. Statistically significant correlations are present only between the number of menstrual cycles in the past year and estradiol levels and progesterone levels.

SRE and Running Stress Scores

The Schedule of Recent Events Score for life events in the past year was similar for all groups of runners, with a mean score for all runners of 323. This value is one associated with an 80% risk of developing an illness in the near future according to Amundson, Holmes and Hart (1981). The high mean score must be interpreted in consideration of the fact that the range of scores and their associated risk factors were developed from a population 18

Table 16

Late Follicular Serum Analysis Means

	All Runners (N=70)	Menstrual Cycles in Past Year: 9+ (n=54)	4-8 (n=7)	0-3 (n=9)	r
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Total serum cholesterol (mg/dl) (Normal = 132-233 mg/dl)	195.0(29.9)	192.0(29.8)	208.0(24.7)	205.0(32.1)	-.17
HDL cholesterol (mg/dl) (Normal = 37-75 mg/dl)	67.0(16.1)	66.0(15.8)	75.0(22.1)	68.0(12.5)	-.14
Total cholesterol/HDL ratio (CHD risk > 5)	2.9	2.9	2.8	3.0	-.04
LDL cholesterol (mg/dl) (Normal = 65-161 mg/dl)	116.0(29.0)	113.0(28.1)	121.0(28.6)	129.0(34.0)	-.14
Triglycerides (mg/dl) (Normal = 42-170 mg/dl)	64.0(21.4)	64.0(22.3)	57.0(10.2)	73.0(20.8)	-.15
Estradiol (pg/ml) (Normal = 50-250 pg/dl)	201.0(160.6)	236.0(162.6)	128.0(94.3)	46.0(19.9)	.40***
Testosterone (pg/ml) (Normal = < 1000 pg/ml)	571.0(173.9)	561.0(157.9)	586.0(139.2)	626.0(278.8)	-.13

Note. r = correlation coefficient with number of menstrual cycles
* = significant at .10 ≥ p > .05
** = significant at .05 ≥ p > .01
*** = significant at .01 ≥ p > .001

Table 17

Mid-Luteal Serum Analysis Means

	All Runners (N=70)	Menstrual Cycles in Past Year 9+ (n=54)	4-8 (n=7)	0-3 (n=9)	r
	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	$\bar{X}$(S.D.)	
Total serum cholesterol (mg/dl) (Normal = 132-233 mg/dl)	192.0(26.7)	190.0(27.8)	202.0(19.1)	202.0(23.8)	-18
HDL cholesterol (mg/dl) (Normal = 37-75 mg/dl)	64.0(15.1)	64.0(15.5)	70.0(19.7)	62.0(8.5)	-.01
Total cholesterol/HDL ratio (CHD risk > 5)	3.0	3.0	2.9	3.3	-.05
LDL cholesterol (mg/dl) (Normal = 65-161 mg/dl)	114.0(25.3)	112.0(25.7)	118.0(29.1)	123.0(20.0)	-.14
Triglycerides (mg/dl) (Normal = 42-170 mg/dl)	70.0(24.6)	69.0(22.0)	69.0(20.1)	75.0(36.8)	-.12
Estradiol (pg/ml) (Normal = 100-250 pg/ml)	205.0(119.4)	235.0(111.2)	137.0(123.1)	86.0(59.4)	.35***
Testosterone (pg/ml) (Normal = < 1000 pg/ml)	603.0(195.5)	592.0(183.2)	653.0(261.7)	626.0(226.7)	-.08
Progesterone (ng/ml) (Ovulatory = greater than 3 ng/ml)	7.3(4.6)	8.7(3.7)	4.7(5.2)	1.0(0.0)	

Note. r = correlation coefficient with number of menstrual cycles
* = significant at .10 $\geq$ p > .05; ** significant at .05 $\geq$ p > .01;
*** = significant at .01 $\geq$ p > .001.

to 65 years old. This study sample included only young women 18-37, most of whom were employed outside the home, involved in job changes, marriage, divorce and other lifestyle changes. Although their mean score is high when interpreted across an entire population, it may be a relatively "normal" score for this age range of women. The running stress score calculated for all runners was also similar for all groups, with a mean score of 10 indicating that most runners perceive running as no more stressful than any other life event. Neither score was significantly related to the number of menstrual cycles in the past year, nor were the scores significantly intercorrelated.

Association Between Body Fat, Serum Lipids, Average Daily Cholesterol Intake and Serum Estradiol

In order to evaluate the hypothesized relationship between body fat, serum lipids, cholesterol intake and serum estradiol, a zero order correlation matrix was first examined (See Table 18). The correlations were, in general, not significant, indicating that these variables, taken individually, explained very little of the variation in serum estradiol levels. To investigate the combined effects of these variables on serum estradiol, a stepwise multiple regression analysis was completed. The daily average cholesterol intake contributed most to the variation in serum estradiol, with a beta weight of .26; the other variables had negligible effects. The adjusted r^2 for the completed analysis, however, was .02, indicating that only 2% of the variation in serum estradiol was

Table 18

Intercorrelations of Variables Associated with Serum Estradiol Levels

Variables	1	2	3	4	5	6
1. Age		-.11	.30**	.19	.19	.40***
2. Body fat (%)			.17	-.08	-.16	-.02
3. Average daily cholesterol intake				-.07	.03	.25**
4. Serum cholesterol[a]					.35***	.09
5. HDL cholesterol[a]						.08
6. Serum estradiol[a]						

Note. [a] = late follicular values
* = significant at .10 $\geq$ p $>$ .05
** = significant at .05 $\geq$ p $>$ .01
*** = significant at .01 $\geq$ p $>$ .001

explained by these variables.

The initial hypothesis did not consider the effects of age on these variables. Since age had significant positive correlations with cholesterol intake and serum estradiol, age was then added to the multiple stepwise regression procedure to assess its effect on variation of serum estradiol levels.

Age explained a majority of variation in serum estradiol levels, while daily average cholesterol intake increased the explained variance by only two percent. As in the previous analysis, the serum lipid levels and percent body fat contributed negligibly to the variation in serum estradiol. The r^2, adjusted for the number of variables and number of subjects, indicated that the set of variables incorporating age explained 12% of serum estradiol variation (See Table 19).

Further Analysis Associated with the Number of Menstrual Cycles Per Year

Although the zero order correlations reported earlier are helpful in examining the associations between variables, correlations generated by multiple regression analysis in which the direct effects of variables can more easily be seen are more useful in investigating a physiological system in which a multitude of variables are constantly interacting with and modifying other variables.

The Biomedical Data Processing best possible subsets regression subprogram using Mallow's Cp criteria for defining "best subset selection" (Frame, 1981, p. 264) was utilized to select the variables which best explain the variation in the number of

Table 19

Results of Multiple Stepwise Regression of Serum Estradiol on Cholesterol Intake, Serum Lipids, Percent Body Fat and Age

Variables entered	R	r^2	Beta	adjusted r^2
Age	.40	.16	.36	
Cholesterol intake	.43	.18	.15	
HDL cholesterol[a]	.43	.18	-.06	
Serum cholesterol[a]	.43	.19	.06	
Percent body fat	.44	.19	-.02	
				.12

Note. [a] = late follicular values

N = 65

menstrual cycles in the past year for this sample. Twenty-five variables with the highest correlations between number of menstrual cycles in the past year and with low intercorrelations were entered in the equation. Due to their clinical relevance and statistical restrictions imposed by the number of subjects involved in the study (65), three sets of three to four variables were selected for further evaluation using SPSS's multiple stepwise regression subprogram. The data generated from that analysis are summarized in Table 20. The adjusted variation explained by these subsets ranges from 32% to 36%. Previous studies have suggested that age, body fat and ponderal index and decreased estrogen levels are associated with menstrual cycle frequency. These variables consistently appear in the results of this analysis. A variable which has not previously been reported as being associated with menstrual regularity, cholesterol intake, predicts the most variation in each one of the subsets.

Path Analysis

Using the physiological model in Figure 1 (page 5), the results of the correlation and regression analyses previously discussed, a path diagram was developed, postulating causal linkages between variables. The correlation coefficients of variables used in the path analysis are included in Table 21. The path analysis was done to more fully examine the relationships among the variables associated with the number of menstrual cycles per year. The exogenous variables included age, average daily cholesterol intake,

Table 20

Results of Multiple Stepwise Regression of Number of Menstrual Cycles in Past Year on Predictor Variables

Three variables subsets	Multiple r	r^2	Adjusted r^2
Cholesterol intake	.46	.21	
Serum estradiol	.55	.30	
Ponderal index	.61	.37	
			.34
Cholesterol intake	.46	.21	
Serum estradiol[a]	.55	.30	
Percent body fat	.59	.35	.32
Cholesterol intake	.46	.21	
Serum estradiol[a]	.55	.30	
Ponderal index	.61	.36	
Age	.64	.40	
			.36

Note. N = 65; [a] = late follicular values

Table 21

Intercorrelations Between Variables Used in Path Analysis

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
1. Age		.33***	.30**	.23*	-.11	.19	.40***	.42***
2. Training time/mile			.24**	.06	.38***	-.03	.22*	.39***
3. Cholesterol intake				.65***	.17	-.07	.25**	.46***
4. Caloric intake					.08	.01	.28**	.39***
5. Percent body fat						-.08	-.02	.28**
6. Serum cholesterol[a]							.09	-.18
7. Serum estradiol[a]								.41***
8. Number of menstrual cycles in past year								

Note. [a] = late follicular values
* = significant at .10 $\geq$ p > .05
** = significant at .05 $\geq$ p > .01
*** = significant at .01 $\geq$ p > .001

caloric intake, and training time per mile. The endogenous variables, theoretically causally linked to the exogneous variables, included percent body fat, serum cholesterol and serum estradiol. The dependent variable was the number of menstrual cycles per year. The adjusted variance explained by this model is 41%.

The pattern of beta weights associated with the postulated causal linkages indicates that this model explains the number of menstrual cycles per year more satisfactorially than it explains the endogenous variables although the endogenous variables contribute to the variation in menstrual cycles. An analysis of the direct (path coefficient) and total indirect (correlation coefficient - path coefficient) effects (Kerlinger & Pedhazur, 1973) of percent body fat, serum cholesterol and serum estradiol in the dependent variable shows that percent body fat and serum cholesterol have primarily direct effects while the effects of serum estradiol on the dependent variable are approximately half direct and half indirect (See Figure 4).

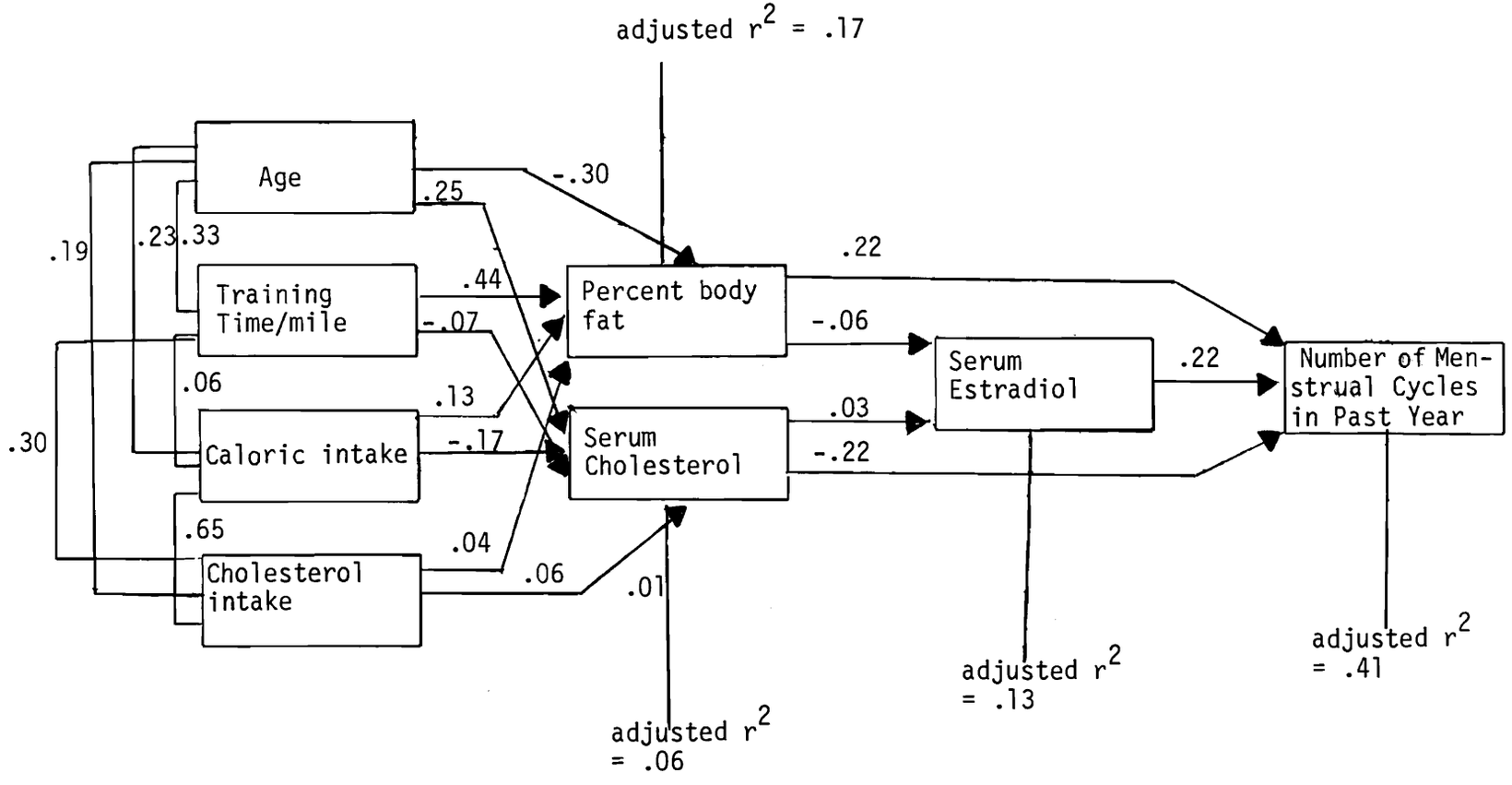

Figure 4. Path analysis diagram

CHAPTER V

DISCUSSION

The picture of the amenorrheic runner that emerges from this study is that of a young woman with a lower than average percent body fat who eats fewer calories, carbohydrates, fats, proteins and cholesterol and who trains at a slightly faster pace, slightly more often than her eumenorrheic counterpart.

The Association of Variables with the Number of Menstrual Cycles in the Past Year

The first research question addressed in this study dealt with the relationships of previously measured variables with the number of menstrual cycles per year. Variables previously cited in the literature as being associated with exercise-induced amenorrhea and supported by this study include younger age at the time of the study, lower body weight, lower percent body fat and training intensity. Factors which may be associated with secondary amenorrhea but which have been reported inconsistently include weight loss and previous menstrual irregularity. In this study, these factors were not significantly correlated with the number of menstrual cycles in the past year. Nulliparity, reported by both Baker et al. (1981) and Dale et al. (1979a) and older age at menarche,

additionally reported by Lutter and Cushman (1982) to be associated with exercise induced amenorrhea were not significantly correlated with the number of menstrual cycles in the past year.

The second research question concerned variables not previously studied relative to their association with menstrual function. Variables not assessed in previous studies which were significantly correlated with menstrual irregularity include average daily intake of calories, carbohydrates, fats, proteins, cholesterol, and average training time per mile. Life stress and running stress were approximated by the SRE questionnaire and the computed running stress score were not significantly correlated with the number of menstrual cycles in the past year.

Age

Age at the time of study has consistently been reported to be lower in amenorrheic athletes, as in this study. A younger age seemed to be associated with nulliparity in other studies, which was not the case in this study. It may be that the fewer years since menarche, the less stable the hypothalamic-pituitary-ovarian axis is, and the more susceptible it is to disruption.

Body Fat and Weight

The mean percent body fat for all runners as estimated in this study is consistent with findings by others (Dale et al., 1979a; Baker et al., 1981).

Percentages in these studies are clearly below Frisch's (1974) postulated threshold of 22% body fat for maintenance of menstrual

cycles, yet 77% of these women have continued to menstruate regularly. It must be recognized that estimation of percent body fat from the indirect method of skinfold thickness measures is imprecise and the group results may have underestimated body fat. It should be noted, however, that the lower percent body fat of the amenorrheic runners is substantiated by a lower body weight and higher ponderal index in these runners. Body weight, particularly when using the same balance scales for all measurements, may be a more precise measure than skinfold thickness although not specific for body fat. When comparing body weights and particularly when the interest is in body fat, it is important that the sample be similar in physical condition, as in this study. A group of physically unconditioned people may have similar weights as a group of conditioned people, but due to exercise their body composition, including body fat percentage, is likely to vary considerably. In this population of physically conditioned runners, both weight and ponderal index were significantly correlated with the number of menstrual cycles per year, consistent with the reports of others (Baker et al., 1981; Lutter & Cushman, 1982).

Weight loss in the past year was not statistically related to menstrual irregularity. Weight loss may be associated with the initiation of anovulation and amenorrhea, and for women amenorrheic for more than one year, this measure did not identify the relationship between weight loss and the onset of amenorrhea. The other major consideration of statistical analysis is that with the average low weight of the amenorrheic runners, the loss of even one or

two kilograms may be of clinical significance while not statistically significant.

The incorporation of the more precise process of hydrostatic or underwater weighing for estimation of body fat percentage should be given serious consideration in future research, particularly if prediction equations relating body fat and menstrual irregularity are to be developed. In a longitudinal study which might follow runners to observe the development of menstrual irregularity, it may not be feasible to hydrostatically weigh each subject at frequent intervals. A more convenient, faster procedure, such as weight, could be done on a daily or weekly basis, with weight changes correlated to changes in percent body fat measured hydrostatically at monthly intervals.

Training Intensity

The association between training intensity and exercise-associated amenorrhea in previous studies has been based on equating intensity with miles run per day or days and weeks run per year. These two variables may more accurately reflect duration and frequency of exercise, while training time per mile appears to be a more precise indicator of intensity of training. Although both training time per mile and days and weeks running were significantly correlated with the number of menstrual cycles in the past year, training time had a stronger association with both the number of cycles and $\dot{V}O_2$ max. Intensity of training may also be related to the physical stress of running as well as to

alterations in blood flow to organ systems, and altered metabolic functions. All these changes may be associated with menstrual irregularity. Future studies need to more clearly define and evaluate training intensity as well as identify and measure changes associated with training intensity and how these variables impact on menstrual function.

Menstrual History

Prior menstrual irregularity and age at menarche were variables not correlated with current menstrual irregularity. These variables are difficult to assess in any study, since they are based on subject recall. Furthermore, researchers must use caution in employing the term "irregularity," as many women interpret irregularity as referring to the varying length of the bleeding phase as opposed to the varying length of the entire menstrual cycle. Sample sizes and the conditions under which the history is elicited may also contribute to the conflicting results reported about these variables.

The reported decrease in frequency of occurrence of cycles and decreased bleeding phase in the eumenorrheic runners, changes regarded as favorable by many women, may indicate an increase in anovulatory cycles even in these women. If this is the case, the phenomenon of exercise-induced anovulation may be even more widespread than previously recognized, particularly since it is difficult to identify anovulation in the absence of amenorrhea. The results of change in menstrual patterns since beginning to run

may, however, be complicated by the use of steroid contraceptives during part of that time interval. This variable needs to be more carefully assessed in future studies.

Nulliparity was not significantly related to exercise-associated amenorrhea in this study. Dale et al. (1979a) and Baker (1981) have suggested that pregnancy may result in maturation of the hypothalamic-pituitary-ovarian axis, thereby "protecting" against amenorrhea; however, this study does not support that conclusion. Although pregnancy may cause some maturation of the female reproductive system, the results of this study suggest that the system remains susceptible to exercise-associated alterations which may result in secondary amenorrhea.

Investigators who have reported significant relationships between menstrual history variables and current menstrual irregularity have suggested that current menstrual irregularity is a result of genetic predisposition rather than an exercise-associated condition. The results of this study indicate that runners may have considerable control over whether or not they develop exercise-induced amenorrhea.

Stress

Stress has frequently been postulated to be associated with secondary amenorrhea. The absence of correlation between either the SRE score or the running stress score and the number of menstrual cycles per year do not support that conclusion. This is the first reported investigation into relationships among

life events, running stress, and current menstrual irregularity, and as such, provides many suggestions for future research efforts.

Holmes and Holmes (1974) stated that the SRE measures life change events; they did not speculate on the relationship between life change and "stress." If stress is, however, defined as a stimulus requiring an adaptive response, then life change could be equated to stress. The major concern with the use of the SRE is that each life event had a predetermined weighted score depending on the magnitude of importance of the event in the population on which the questionnaire was developed. The assumption that degree of change caused by life events is the same for all people may not be valid. Future studies which investigate life stress in runners need to explicitly define stress and seek more sensitive measures of stress. Use of types of life events included on the SRE with a Likert scale to allow individual evaluation of each event, may provide more accurate information.

The lack of significant correlation between the running stress score and current menstrual irregularity may be due to the questions asked concerning the participants' perception of running stress. The running stress questions need to be improved, using scale development and factor analysis techniques. An evaluation of the impact of competitive running versus non-competitive running needs to be incorporated into this scale or questionnaire as well as attention to perceived psychological as opposed to physiological stress. The word "stress" has a variety of meanings, a point

of concern about the questions asked regarding running "stress" in this study.

Future studies also need to consider other variables which affect perceptions of "stress," such as personality characteristics as well as physiological variables, including endorphin levels, current fitness level and past injury history. It may be that even with more intense investigation, the preliminary findings of this study indicating that there is no correlation between life change, running stress and menstrual irregularity will be supported.

Nutritional Assessment

Each of the nutritional variables considered was significantly related to the number of menstrual cycles in the past year. The intake of calories, fats and cholesterol in the amenorrheic group was extremely low, although their average nutritional assessment score indicates an average intake of vitamins and minerals, similar to the other runners.

Information on cholesterol intake contained in the nutritional assessment received by each participant mentions the association between cholesterol intake and heart disease. A dramatic reduction in cholesterol levels below the RDA is not advised, however, due to the many interactive effects in which cholesterol is involved and the unknown effects dietary cholesterol may have. The reduction in frequency of ovulation to the point of amenorrhea may be an example of the effects of significant reduction

in cholesterol intake in women.

Although the results of this study do not show a causal relationship between cholesterol intake and menstrual function, the effects of dietary cholesterol intake in amenorrheic runners should be evaluated.

Laboratory Results

The amenorrheic runners were hypoestrogenic with progesterone levels supporting their anovulatory condition. All runners had testosterone levels within normal limits. This hormonal picture is consistent with the findings of Dale et al. (1979a) and Baker et al. (1981). The lipid profiles are similar for all runners, in spite of differences in dietary cholesterol intake and hormonal status. This suggests that there may be some physiological mechanism which regulates cholesterol metabolism and maintains a stable serum cholesterol intake. Furthermore, when dietary cholesterol intake is decreased in physically conditioned women, serum cholesterol may be maintained at the expense of steroid hormone metabolism. These speculative relationships require more intense investigation.

It has also been speculated that hypoestrogenic athletes may share the increased risk of ischemic heart disease experienced by hypoestrogenic post-menopausal women. This study does not lend support to that hypothesis since all runners had high HDL-cholesterol levels and low total cholesterol/HDL cholesterol ratios. If high levels of HDL-cholesterol continue to be asso-

ciated with low risk of development of ischemic heart disease, then even premenopausal hypoestrogenic runners should continue to be at similar low risk as premenopausal runners with normal estrogen levels. This needs to be evaluated in further longitudinal studies.

Evaluation of Multiple Variables

The best possible subsets analysis allowed multiple variables to be considered simultaneously to determine the combination of variables which explained the most variance in the number of menstrual cycles per year. Of significance in this analysis was for each subset, the variable explaining the most variation in number of menstrual cycles was cholesterol intake. This variable is one which is easily modified by alterations in dietary intake.

Serum estradiol was also associated with the number of menstrual cycles. It is unclear whether the hypoestrogenic state causes anovulation or anovulation results in hypoestrogenism. These relationships need to be investigated in more detail.

Evaluation of the Relationships Among Body Fat, Serum Cholesterol, Dietary Cholesterol, and Serum Estradiol

The variables of body fat, serum cholesterol and dietary cholesterol are associated with the number of menstrual cycles per year, but not with variation in serum estradiol levels, as indicated by both the multiple regression and path analysis.

Wentz's (1980) hypothesis that decreased body fat results

in decreased sites for aromatization of androgens to estrogens, causing the decreased serum estrogen levels is not supported. The mechanisms by which body fat and both cholesterol intake and serum cholesterol exert their effects on the number of menstrual cycles per year remain to be explained. These mechanisms may involve biochemical alterations and interactions too minute or subtle for measures used in this study or may involve variables not measured by this study. This area remains to be investigated.

Path Analysis

The path analysis lends support to the theoretical formulation that body fat and serum cholesterol may be causally related to menstrual function, but it does not support the hypothesis that body fat and serum cholesterol exert their effect on the number of menstrual cycles per year through alterations in serum estradiol. When the 50% direct - 50% indirect effect of serum estradiol on the dependent variable is considered in conjunction with the small amount of variance in serum estradiol explained by body fat and serum cholesterol, the importance of other factors in regulating estradiol levels becomes apparent. Other factors are probably the central nervous system hormones GnRH, LH, FSH and other biochemical mediators and neurotransmitters such as dopamine, norepinephrine, catecholestrogens and endorphins (See Figure 2). The mechanisms by which body fat and serum cholesterol exert direct effects on the dependent variable remain to be explained.

Other aspects of the path analysis concern the path coefficients of the exogenous variables linked to percent body fat and serum cholesterol. Training time per mile and age have the greatest direct effects on percent body fat although in opposite directions. The effect of training time per mile on percent body fat is particularly important, since this is a variable immediately modifiable by a change in behavior. Age and cholesterol intake have the greatest direct effect on serum cholesterol, although the effects are not as strong as those associated with body fat. As might be expected from path coefficients, the variance explained by this set of variables is greater for percent body fat (17%) than for serum cholesterol (6%).

The model derived from the path analysis offers a beginning theoretical framework within which a limited number of variables and their hypothesized causal effects were evaluated. Approximately 40% of the variation in the number of menstrual cycles per year is explained. The analysis is limited due to the sample size of 65 and because, as with any path analysis used in a non-experimental design employed for explanation, causal unidirectional flow was assumed from prior physiological and theoretical considerations.

This analytic method has two major drawbacks in examining the range of physiologic variables which regulate reproductive function: a) the large number of variables involved would require a very large sample size, and b) the introduction of feedback influences, such as those involved at the central nervous system,

would involve reciprocal causation, isolating the unidirectional causal flow requirement associated with path analyses.

Implications

The implications of this study for nursing practice are concerned primarily with the advice nurses may provide women who exercise and who wish to avoid the development of menstrual irregularity. As women undertake exercise programs, they should be advised to maintain an adequate nutritional intake, including the recommended daily allowance of dietary cholesterol. Women who have exercise-associated menstrual irregularity should be advised that studies have not been done to assess the effects of modifying certain behaviors on the resumption of regular menstrual patterns. Anecdotal reports (Dale et al., 1979a; Baker et al., 1981) indicate that women who stop running may resume ovulation. The results of this study suggest less drastic measures may be effective. An increase of nutrient intake, including cholesterol, and a decrease in training time per mile, may be effective in achieving menstrual regularity. Younger women must be particularly attentive to their nutritional intake as younger age is a non-modifiable variable associated with exercise-induced amenorrhea. Women who are hypoestrogenic due to exercise associated amenorrhea should understand that the long term effects of hypoestrogenism on young physically active women have not been evaluated but it appears that hypoestrogenism in this population does not alter the favorable lipid profile achieved thorugh exercise.

The implications for nursing education are concerned primarily with the orientation of nursing curricula to health behaviors and information to be provided about such behaviors. As nursing curricula incorporate health maintenance and illness prevention concepts, there is an increased need for information concerning the outcomes of health behaviors. As illustrated by this study, these outcomes can be both expected and desired, for example, increased HDL levels, and unexpected or even undesired, such as amenorrhea. Nurses need to be aware that there may be undesirable outcomes even with generally accepted health practices such as exercise.

The implications for nursing research center around the need for more intense investigation by nurses of a healthy population. As health promotion becomes a more important social, financial and political issue, investigation of health behaviors and outcomes of health practices must occur. Since nurses have historically been concerned with health promotion, this is an acceptable area for concerted research efforts by nurses.

Recommendations for Future Research

The recommendations for future research discussed earlier are summarized as follows:

1. incorporation of more precise measures to evaluate body fat, training intensity, menstrual history and stress;

2. evaluation of effects of training intensity on variables which may affect menstrual function;

3. investigation of the mechanisms which mediate the effects of measured variables on the number of menstrual cycles per year;

4. longitudinal studies of the long term effects of exercise associated hypoestrogenism, and

5. continued recruitment of large samples so that regression analysis can be used in answering research questions concerning relationships among variables related to exercise-associated amenorrhea.

APPENDIX A

COVER LETTER, INSTRUCTIONS TO PARTICIPANTS,

SUBJECT IDENTIFICATION FORM

AND PERSONAL DATA FORM

Emory University School of Medicine

Thomas K. Glenn Memorial Building

69 Butler Street, S.E. Atlanta, Georgia 30303

Department of Gynecology
and Obstetrics

Dear Friend:

Thank you for agreeing to participate in this study of women runners. Your participation will add greatly to the knowledge we have concerning the effects of exercise on women, in addition to helping our understanding of factors affecting the menstrual cycle, I hope you will also experience some personal benefit from participation, most especially an increased amount of information about your own physiological status.

This packet includes an instruction sheet, two questionnaires and a diet diary. Please read over the instruction sheet when you get this, so that if you have questions, you can give me a call. A sample of the informed consent form you will be asked to sign is also enclosed.

I am looking forward to meeting you soon, if I have not already done so. Again, many thanks for agreeing to participate, and don't hesitate to call if you have any questions.

Sincerely,

Patty Gray, R.N., M.S.N.

Instructions to Participants

Please read this sheet first. If you have any questions after reading this sheet and after looking over the questionnaires, please do not hesitate to give me a call (588-3628). Again, thanks for agreeing to participate in the study.

Questionnaires

What would a study be without a few questionnaires to fill out? There are two questionnaires and a diet diary in this packet.

The first questionnaire is a history questionnaire, asking about your reproductive and running history. There are specific instructions on this form about its completion. There are questions about your menstrual history on this form, from the time you began to have menstrual periods. I know it may be difficult to remember these details; please try and remember as much as you can, as accurately as possible. Please look over the entire questionnaire first, before you answer any questions. Let me know if anything is not clear. I will go over the form with you at your first blood sampling appointment. If possible, please complete this questionnaire and bring it with you to your first appointment.

The second questionnaire is the Schedule of Recent experiences form. Again, there are instructions for the completion of this form at the beginning of the form. This questionnaire identifies stressful life events which may affect the regularity of your menstrual cycle. Along with your history questionnaire, please complete this form and bring it to your first appointment.

The diet diary is also included in this packet. Please read the instructions in the front of the diary about its use. You are asked to fill out the diary in two day segments, the first two days being prior to your first blood sample and the next two days prior to your second blood sample, for a total of four days. After the analysis of your diary is completed, Margaret Peterson, an Emory University dietician, will be happy to see you individually for a nutritional consultation if you so desire (329-6766). Please bring your diet diary to both blood sample appointments.

Your honest and thoughtful attention to these questionnaires will have great bearing on the outcome of this study; please try and be as accurate as possible, and if a question is unclear, please contact me.

Skinfold Thickness Measures

This is one part of the study that does not require any effort or energy on your part. It simply involves the use of skinfold calipers to measure your skinfold thickness, from which your percent body fat is estimated. This procedure, which is very brief, can be done either at the blood sample appointment or at the stress testing, whichever is more convenient for you.

Stress Testing

This test involves walking/running on a motor driven treadmill until you reach 80% of your age-predicted heart rate. This will be done at Georgia State University, with appointments scheduled on Saturday if possible (if not, other arrangements will be made). Trained medical personnel will be present in the unlikely event any medical problems arise. You do not have to do any special preparation for this test; you may want to eat a light meal an hour or two prior to the test. It is usually not advisable to do this type test with either an empty or full stomach.

Blood Samples

Blood samples will be collected twice, with ten days between each sample. The first sample will be collected on the 11-14th day of your cycle, with the second drawn on the 21-24th day of your cycle (day 1 of your cycle is the first day of the bleeding phase). If your cycle is very long or very short, or you do not have menstrual periods, adjustments will be made in scheduling your appointments according to your cycle.

Please call me during the bleeding phase of your next cycle to set up your blood sample appointments. Please let me know as soon as you receive this if you do not have regular cycles or you do not have cycles at all, and we will go from there in setting up your appointments.

The blood samples will be analyzed for a variety of substances, including estrogen levels, cholesterol (HDL and LDL) and triglycerides. Your blood levels of cholesterol are very sensitive to what you have been eating, so you will have your blood drawn first thing in the morning, BEFORE you eat breakfast. Things like alcohol (beer, wine and mixed drinks) fish and Vitamin B also affect blood cholesterol levels, so please avoid alcohol, fish and vitamin B the day BEFORE your blood sampling appointments.

Your appointment for the blood sample will be individually arranged with me, according to your menstrual pattern, and will hopefully cause as little inconvenience to you as possible. Please do remember to call me during the bleeding phase of your next cycle, to make

the necessary arrangements.

For your records:

_____ Date of first blood sample appointment (remember the history and diet questionnaires)

_____ Date of second blood sample appointment (remember the diet questionnaire)

_____ Date for stress testing

Again, if you have questions about anything relating to your participation in this study, or if I can be of help in any other health-related matter, please feel free to contact me (588-3628).

Subject Identification Form

Subject #_____

Subject Name_____

Address_____

Phone_____(home)_____

_____(work)_____

Nearest relative/person to contact in case of emergency:

Name_____

Address_____

Phone _____

Address through which you may always be reached:

_____

_____

_____

Subject # _____ Personal Data Form

Birthdate _____/_____/_____
month day year

Highest degree held:

1. High school
2. Baccalaureate
3. Masters
4. Doctorate

Current occupation

1. Artist
2. Banker/stock broker
3. Educator
4. Engineer
5. Health professional
6. Housewife
7. Lawyer
8. Musician
9. Politician
10. Sales
11. Secretary
12. Social worker
13. Student
14. Technician
15. Writer
16. Other_____

How long have you been running on a regular basis:

1. Less than 1 year
2. 1-2 years
3. 3-4 years
4. 5 years or more

How long have you been running your current mileage?_____

Have you ever run a marathon?

1. Yes
2. No

Are you training to run a marathon?

1. Yes
2. No

Have you ever competed in a race of lesser distance than a marathon?

1. Yes
2. No

APPENDIX B

CONSENT FORM

Informed Consent Form

I understand the purpose of this study is to examine the relationships that may exist between body composition, serum lipids and ovarian hormones in women runners using four standard procedures: a) venipuncture to obtain blood samples, b) submaximal stress testing to calculate the level of cardiovascular endurance, c) measurement of skinfold thickness using skinfold calipers to calculate percent body fat; and d) completion of two questionnaires and a diet diary. I understand that my involvement in this study will involve approximately three hours of my time. The venipuncture may involve minimal discomfort. The skinfold measures may involve partial disrobing for a short period of time. Privacy will be provided for this procedure. I have had the possible complications of submaximal stress testing explained to me and I understand that there is very minimal physical risk associated with this procedure. I understand that I will be asked to provide information about previous menstrual history and other significant life events and also to provide a diet log of my food and beverage intake.

All questions I had about participation in this study have been answered to my satisfaction. I understand all information will be kept confidential and will be number coded to protect my identity.

I understand that the direct benefits to me will include knowledge of the results from submaximal stress testing and blood testing which will be done free of charge to me. I understand that I will have an opportunity to discuss the results of my individual tests with Patty Gray, R.N. and/or other consultants on this research project. I understand that a written report of this study will be made available to me upon completion of this study.

I am not being compensated for my participation in this study.

I understand that my participation is entirely voluntary and that I may withdraw at any time without prejudice or penalty.

I understand that Emory University will assume no financial responsibility or liability for any medical treatment that may be required by my participation in this study.

Signatures

_____ _____

Subject date

_____

Witness

This consent form contains no exculpatory language through which the subject is made to waive any of her legal rights or to release the institution from liability for negligence.

_____

Investigator

APPENDIX C

SCHEDULE OF RECENT EXPERIENCES

AND HISTORY QUESTIONNAIRE

Schedule of Recent Experiences*

Subject #_____

INSTRUCTIONS: For each event listed below, please do the following:

Think back on the event and decide if it happened during the last 12 months. If the event happened, indicate the number of times it happened by placing a number in the column labeled 0-12 months ago. If the event did not happen, leave the space blank.

		0-12 months ago
1.	A lot more or a lot less trouble with the boss	_____
2.	A major change in sleeping habits (sleeping a lot more or a lot less or change in the part of the day when sleeping)	_____
3.	A major change in eating habits (a lot more or a lot less food intake, a different meal hours or surroundings)	_____
4.	A revision of personal habits (dress, manner, associations, etc.)	_____
5.	A major change in the usual type of or amount of recreational activities	_____
6.	A major change in social activities	_____
7.	A major change in church activities	_____
8.	A major change in number of family get-togethers	_____
9.	A major change in financial state (a lot better or a lot worse off than usual)	_____
10.	Trouble with in-laws	_____
11.	A major change in the number of arguments with spouse (either a lot more or a lot less)	_____
12.	Sexual difficulties	_____

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13. Major personal injury or illness _____

14. Death of a close family member, other than spouse _____

15. Death of spouse _____

16. Death of close friend _____

17. Gaining a new family member (through birth, adoption, oldster moving in, etc.) _____

18. Major changes in the health or behavior of a family member _____

19. Change in residence _____

20. Detention in jail or other institution _____

21. Minor violations of the law (traffic tickets, disturbing peace, etc.) _____

22. Major business readjustment (merger, bankruptcy, reorganization, etc.) _____

23. Marriage _____

24. Divorce _____

25. Marital separation from spouse _____

26. Outstanding personal achievement _____

27. Son or daughter leaving home (marriage, attending college, etc.) _____

28. Retirement from work _____

29. Major change in working hours or conditions _____

30. Major change in responsibilities at work _____

31. Being fired from work _____

32. Major change in living conditions _____

33. Spouse beginning or ceasing work outside home _____

34. Taking out a loan or a mortgage for a major purchase (home, business, etc.) _____

35. Taking out a loan or mortgage for a lesser purchase (i.e., car freezer, TV, etc.) _____

36. Foreclosure on a mortgage or loan _____

37. Vacation _____

38. Changing to a new school _____

39. Changing to a different line of work _____

40. Beginning or ceasing formal schooling _____

41. Marital reconciliation with mate _____

42. Pregnancy _____

History Questionnaire

Subject #_____

Please answer the following questions by circling the number beside the answer that best fits your situation. If none of the answers fit your situation, please indicate this by writing your answer below the question.

1. At what age did you begin having menstrual periods?

    1. While 10 years old or younger
    2. While 11 years old
    3. While 12 years old
    4. While 13 years old
    5. While 14 years old
    6. While 15 years old
    7. While 16 years old or older
    8. Have not started having menstrual periods (Go to question 26)
    9. Cannot remember at all

2. At that time, how much did you weigh?

    1. Less than 70 lbs.
    2. 70-80 lbs.
    3. 81-90 lbs.
    4. 91-100 lbs.
    5. 101-110 lbs.
    6. 111-120 lbs.
    7. 121-130 lbs.
    8. Greater than 130 lbs.
    9. Cannot remember at all

3. At that time, how tall were you?

    1. Less than 5 feet tall
    2. 5'0" to 5'3" tall
    3. 5'4" to 5'7" tall
    4. 5'8" to 5'11" tall
    5. 6 feet tall or taller
    6. Cannot remember at all

(See next page)

The following set of questions have two sets of answers, with each set applying to a different time interval. The first interval, with answers found in the first column, is the time from when you started your menstrual periods until you were 18 years old. The second interval, with answers in the second column, is from when you were 18 years old until you started running on a regular basis. Under the column headings, you are asked to fill out the appropriate dates for your situation. If you have not started having menstrual periods, you do not have to fill out this section; go to question 26. If you started running at 18 or younger, you do not have to fill out the second column of answers; please do fill out the answers in the first column.

	For the Time Interval From the Time you Started Your Periods Until you were 18 years old (from __/____ to ____/_____) mo. yr. mo. yr.	For the Time Interval From the time you were 18 years Until you started running (from ____/____ to ____/____) mo. yr. mo. yr.
4. How long did your menstrual cycles last (from beginning of one bleeding phase to the beginning of the next bleeding phase?)	(2) 1. Less than 14 days (1) 2. 14-21 days (1) 3. 22-36 days (2) 4. Greater than 36 days (3) 5. Too irregular to describe 6. Cannot remember at all	(2) 1. Less than 14 days (1) 2. 14-21 days (1) 3. 22-36 days (2) 4. Greater than 36 days (3) 5. Too irregular to describe 6. Cannot remember at all
5. Please describe the regularity of your menstrual cycle	(1) 1. Very regular (2) 2. Slightly irregular (3) 3. Very irregular 4. Cannot remember at all	(1) 1. Very regular (2) 2. Slightly irregular (3) 3. Very irregular 4. Cannot remember at all
6. How many days did your bleeding phase last?	(1) 1. 1-3 days (1) 2. 4-7 days (3) 3. 8 days or longer 4. Cannot remember at all	(1) 1. 1-3 days (1) 2. 4-7 days (3) 3. 8 days or longer 4. Cannot remember at all

	For The Time Interval From the Time You Started Your Periods Until you Were 18 Years Old	For the Time Interval From The Time You Were 18 Years Old Until you Started Running
6. Describe the amount of blood flow you generally had:	1. Light 2. Moderate 3. Heavy 4. Too variable to describe 5. Cannot remember at all	1. Light 2. Moderate 3. Heavy 4. Too variable to describe 5. Cannot remember at all
7. Did you experience pain or discomfort with your monthly periods, in general:	1. Severe pain that interfered with daily activity 2. Moderate pain that did not interfere with daily activity 3. Minimal discomfort 4. Occurrence of pain is variable 5. No discomfort	1. Severe pain that interfered with daily activity. 2. Moderate pain that did not interfere with daily activity 3. Minimal discomfort 4. Occurrence of pain is variable 5. No discomfort
8. Did you use birth control pills?	1. Yes, from____ to____ 2. No	1. Yes, from ____ to ____ 2. No
9. Did you use an IUD?	1. Yes, from ____ to ____ 2. No	1. Yes, from____ to____ 2. No
10. Did you take medication to induce ovulation or menstrual flow?	1. Yes 2. No	1. Yes 2. No

	For The Time Interval From the Time You Started Your Periods Until you were 18 Years Old	For The Time Interval From The Time You Were 18 Years Old Until You Started Running
11. Were you pregnant?	1. Yes 2. No	1. Yes 2. No
12. Did you have gynecologic surgery?	1. Yes _____ describe 2. No	1. Yes _____ describe 2. No

(Go to the next page, please)

The remainder of the questions are only asked once. Please answer these questions, adding comments below the questions.

13. Did the frequency of your menstrual periods change after you started running?

1. Yes, increased in frequency
2. Yes, decreased in frequency
3. No, stayed the same

14. If the frequency of your periods changed, can you associate that change with any of the following (check all that apply):

1. Weight change
2. Taking hormones (like the pill)
3. Increased life stress
4. Increased mileage
5. Other_____

15. Has the amount of blood flow you have during your menstrual periods changed since you started running?

1. Yes, increased
2. Yes, decreased
3. No

16. Has the amount of discomfort you experience with your menstrual periods changed since you started running?

1. Yes, increased
2. Yes, decreased
3. No, no change

17. Since you have been running, have you been pregnant?

1. Yes, _____times
2. No, have not tried to get pregnant
3. No, have tried, but have not initiated a pregnancy

18. If you have been pregnant since you started running, please indicate the dates of your pregnancies:

1. Have not been pregnant
2. From_____to_____(#1)
   From_____to_____(#2)
   From_____to_____(#3)

19. If you were pregnant since you have been running, were you running regularly at the time of conception:

1. Have not been pregnant
2. Yes, _____ miles per week
3. No, was not running

20. If you were pregnant since you have been running, did you run during the pregnancy?

1. Have not been pregnant
2. Yes, ____ miles per week for ____ months of pregnancy
3. No, did not run

21. If you were pregnant since you have been running, what was the outcome of the pregnancy?

1. Have not been pregnant
2. Miscarriage or abortion
3. Premature infant
4. Full term infant
5. Stillborn infant

22. In the past year, how long did your monthly cycles last, on the average (from the beginning of one bleeding phase to the beginning of the next bleeding phase?)

1. Less than 14 days
2. 14-21 days
3. 22-36 days
4. Greater than 36 days
5. Too variable to describe

23. In the past year, how regular were your menstrual cycles?

1. Very regular
2. Slightly irregular
3. Very irregular

24. Have you ever been evaluated for infertility?

1. Yes, results_____
2. No, have not felt a need for such an examination
3. No, have thought about it, but haven't gotten around to it.

25. Has your partner ever been evaluated for infertility?

1. Yes, results_____
2. No

The next set of questions relate to your running history. If you do not run, go to question 38.

26. In the past year, how many miles per day, on the average, did you run?

1. 1-5
2. 6-10
3. 11-15
4. Greater than 15

27. What was your average time per mile run, in the past year?

1. 6 minutes
2. 6.1 to 8.0 minutes
3. 8.1 to 10 minutes
4. 10.1 minutes or more

28. How many days of the week, on the average did you run?

1. 1-3 days
2. 4-5 days
3. 6-7 days

29. How many weeks of the year did you run, in the past year?

1. 1-24 weeks
2. 25-36 weeks
3. 37-44 weeks
4. 45-52 weeks

30. Did you compete in any marathons during the past year?

1. None
2. 1-2
3. 3-4
4. 5 or more

31. Did you compete in any 10K races during the past year?

1. None
2. 1-3
3. 4-7
4. 8 or more

32. If you stopped running during the year, what was the major reason?

1. Pregnancy
2. Injury_____
3. Other health reason_____
4. Lack of time
5. Lack of interest
6. Other_____

33. What is your current weekly mileage?

1. 30-40 miles per week
2. 41-50 miles per week
3. 51-60 miles per week
4. 61-70 miles per week
5. 71-80 miles per week
6. 81 miles or more per week

34. Are you currently in training for a marathon?

(4pts) 1. Yes, for the past _____ months
(1pt) 2. No

35. Do you feel running (not racing) is stressful?

(3) 1. Yes, but only physically
(3) 2. Yes, but only mentally
(4) 3. Yes, mentally and physically
(2) 4. It depends_____
(1) 5. No

36. Do you feel racing is stressful?

(3) 1. Yes, but only physically
(3) 2. Yes, but only mentally
(4) 3. Yes, mentally and physically
(2) 4. It depends_____
(1) 5. No

37. If you find running stressful, how would you compare it to the other stresses in your life?

(2) 1. I don't find running stressful
(1) 2. Running is less stressful than the other stresses in my life.
(3) 3. Running is about as stressful as any other stress in my life.
(4) 4. Running is more stressful than the other stresses in in my life.

The remainder of the questions relate to other physical activities, weight and medications. EVERYONE should answer these.

38. During the past year, were you involved in any regular exercise activity, besides running?

1. Yes,_____for_____ hours per week.
2. No

39. Are you currently involved in any regular physical exercise activities besides running?

1. Yes,_____for_____ hours per week.
2. No

40. Please describe your weight during the past year (describe the overall pattern; don't include temporary weight changes due to pregnancy):

1. Gained_____ lbs.
2. Stayed the same
3. Lost_____ lbs.

41. Were you on a special diet during the past year?

1. No, not on a special diet
2. Yes, reduced calorie diet
3. Yes, calorie supplemented diet
4. Yes, other special diet_____

42. Please describe any medications you took on a regular basis during the past year?

1. Pain medicine_____
2. Birth control pills; from_____to _____
3. Other hormones;_____
4. Vitamins_____
5. Other_____

If there are additional comments or information about yourself that you would like to share, please attach them on a separate page.

REFERENCES

Adams, C. (Ed.). Symposium on exercise and the heart. American Journal of Cardiology, 1972, 713-736.

Adner, M. & Castelli, W. Elevated high density lipoprotein levels in marathon runners. Journal of the American Medical Association, 1981, 243 (6), 534-536.

Allain, C.C, Poon, L.S., Chan, C.S., Richmond, W., & Fur, P.E. Enzymatic determination of total serum cholesterol. Clinical Chemistry, 1974, 20 (4), 470-475.

Altekruse, E.B., & Wilmore, J.H. Changes in blood chemistry following a controlled exercise program. Journal of Occupational Medicine, 1973, 15 (2), 110-115.

American College of Sports Medicine. Opinion statement on the participation of the female athlete in long distance running. Medicine and Science in Sports, 1979, ix-xi.

American College of Sports Medicine. Guidelines for graded exercise testing and exercise prescription (2nd Ed.). Philadelphia: Lea and Febiger, 1980.

Amundson, M.E., Holmes, T.H., & Hart, C.A. Manual for the schedule of recent experiences. Seattle, Washington: University of Washington School of Medicine, Department of Psychiatry and Behavioral Sciences, RP-10, 1981.

Baker, E.R. Menstrual dysfunction and hormonal studies in athletic women: A review. Fertility and Sterility, December 1981, 36 (6), 691-696.

Baker, E.R., Mathur, R.S., Kirk, R.F. & Williamson, H.O. Female runners and secondary amenorrhea: Correlation with age, parity, mileage and plasma hormonal and sex hormone binding globulin concentrations. Fertility and Sterility, August 1981, 36 (2), 183-187.

Billewicz, W.Z., Fellowes, H.M., & Hytton, C.A. The critical fat hypothesis. Annals of Human Biology, 1976, 3, 51.

Bonen, A., Ling, W.Y., MacIntyre, K.P., Neil, R., McGrail, J.C. & Belcastro, A.N. Effects of exercise on the serum concentrations of FSH, LH, progesterone and estradiol. European Journal of Applied Physiology and Occupational Physiology, 1979, 42, 15-25.

Brisson, C., Valley, M., DeCarufel, D., Deharnais, M., & Tanaka, M. Exercise induced association of the blood prolactin re-

sponse in young women according to the sports habits. Hormone and Metabolism Research, 1980, 12, 201-208.

Brozek, J., Grande, J., Anderson, T., & Keys, A. Densitometric analysis of body composition: Revision of some quantitative assumptions. Annals of the New York Academy of Sciences, 1963, 110, 113-140.

Bucolo, G., & David, H. Quantitative determination of serum triglycerides by the use of enzymes. Clinical Chemistry, 1973, 19 (5), 476-482.

Burnstein, M. Rapid method for the isolation of lipoproteins from human serum by precipitations with polyanions. Journal of Lipid Research, 1970, 11, 583-585.

Cameron, E.H., & Scarisbrick, J.J. Radioimmunoassay of plasma progesterone. Clinical Chemistry, 1973, 19, 253-258.

Campbell, D.E., & Lumbsden, T.B. Serum cholesterol concentration during physical training and subsequent detraining. American Journal of Medical Sciences, 1967, 253, 155-162.

Carlberg, K.A., Buckman, M.T., Peake, G.T., & Riedesel, M.L. Low body weight increases susceptibility to athletic oligo-amenorrhea (Abstract). Fertility and Sterility, 1980, 34, 306.

Carlberg, K.A., Buckman, M.I., & Peake, G.T. Prolactin response to exercise in oligo-amenorrheic and menstruating athletes (Abstract). Panamerican Congress and International Course on Sportsmedicine and exercise science, Miami, Florida, 1981, p. 7.

Carlberg, K.A., Peake, G.T., Buckman, M.I., Srivastava, L.S., & Riedesel, M.L. Pituitary-ovarian axis in oligo-amenorrheic athletes. Federation Proceedings, 1981, 40 (3), 396.

Carlberg, K.A., Peake, G.T., Buckman, M.I., & Srivastava, L.S. Androgen response to exercise in oligo-amenorrheic and menstruating athletes. Program and abstracts, The 63rd Annual Meeting of the Endocrine Society, June 17-19, 1981.

Carlberg, K.A., & Riedesel, M.L. Athletic training and body composition as factors in secondary amenorrhea. The Physiologist, 1979, 22, 17.

Cooper, K.H. The aerobics way. New York: Bantam Books, 1978.

Cunningham, D.S., & Hill, J.S. Effect of training on cardiovascular response to exercise in women. Journal of Applied Physiology, 1975, 39, 891-895.

Dale, E., Gerlach, D., Martin, D.E., & Alexander, C.R. Physical fitness profiles and reproductive physiology of the female distance runner. Physician and Sportsmedicine, 1979, 7, 83-89 (a).

Dale, E., Gerlach, D., & Wilhite, A. Menstrual dysfunction in distance runners. Obstetrics and Gynecology, 1979, 54, 47-54.(b).

Dale, E., & Goldberg, D.L. Implications of nutrition in athletes' menstrual cycle irregularities. Unpublished manuscript, 1981.

Demers, L.M., Harrison, T.S., Halbert, D.R., & Santen, R.J. Cited in P. Gunby, Increasing numbers of physical changes found in the nation's runners. Journal of the American Medical Association (Medical News), 1981, 245, 547.

Drinkwater, B.L. Physiological responses of women to exercise. In J.H. Wilmore (Ed.), Exercise and sports science reviews. (Vol. I). New York: Academic Press, 1973, pp. 125-153.

Eddy, D.O., Sparks, K.L., & Adelizi, D.A. The effect of continuous and interval training in women and men. European Journal of Applied Physiology, 1977, 37, 83-92.

Enger, S.C., Herbjornsen, K., Erkssen, J., & Fretland, H. HDL and physical activity. Scandinavian Journal of Clinical Investigation, 1977, 37, 251-253.

Erdelyi, G. Gynecological survey of female athletes. Journal of SportsMedicine and Physical Fitness, 1962, 2, 174-178.

Erdelyi, G. Effects of exercise on the menstrual cycle. Physician and Sportsmedicine, 1976, 4, 79-83.

Evrard, J.R., Buxton, B.H., & Erikson, D. Amenorrhea following oral contraception. American Journal of Obstetrics and Gynecology, 1976, 124, 88-91.

Feicht, C.B., Johnson, T.S., Martin, B.J., Sparkes, K.E. & Wagner, W.W. Secondary amenorrhea in athletes. Lancet, 1978, 2, 1145-1146.

Fishman, J., Boyar, R.M., & Hellman, L. Influence of body weight on estradiol metabolism in young women. Clinical Endocrinology and Metabolism, 1975, 41, 989-995.

Fishman, J., & Norton, B. Catecholestrogen formation in the central nervous system of the rat. Endocrinology, 1975, 96, 1054-1960.

Flint, M.M., Drinkwater, B.L., Wells, C.L., & Horvath, S.M. Validation of estimating body fat of females: Effect of age and fitness. Human Biology, 1977, 49 (4), 559-572.

Frame, J. Biomedical data processing software (1981 Ed.). Los Angeles: University of California Press, 1981, p. 264.

Fringer, M.N., & Stull, G.A. Changes in cardiorespiratory parameters during periods of training and detraining in young adult females. Medical Science and Sports, 1974, 6, 20-25.

Frisch, R.E. Menarche and fatness: Reexamination of the critical body composition hypothesis. Science, 1978, 200, 1506-1513.

Frisch, R.E., & MacArthur, J.W. Menstrual cycles: Fatness as a determinant of minimum weight for height necessary for their maintenance or onset. Science, 1974, 185, 959-962.

Gordon, T., Kannell, W.B., & Castelli, W.P. Lipoproteins, cardiovascular disease and death. Archives of Internal Medicine, 1981, 141, 1128-31.

Harris, D.V. Quoted in (Journal Eds.), Secondary amenorrhea linked to stress. Physician and Sportmedicine, October, 1978, 6, 24.

Harrison, W. (Ed.). Principles of internal medicine. New York: McGraw Hill Book Company, 1974.

Hoffman, A.A., & Goss, F.A. Effects of an exercise program on plasma lipids of Senior Air Force officers. American Journal of Cardiology, 1967, 20, 516-524.

Hollozy, J.O., Skinner, J.S., Toro, G., & Cureton, T.K. The effects of a six month program of endurance exercise on serum lipids of middle aged men. American Journal of Cardiology, 1964, 14, 753-60.

Holmes, T.H., & Holmes, T.S. The consequence of change for health: How change can make you ill. Blueprint for Health, 1974, 25 (1), 66-75.

Holmes, T.H., & Masuda, M. Life change and illness susceptibility. Separation and Depression, 1973, 161-186.

IL cholesterol test package insert, Cholesterol 35179. Lexington, Massachusetts: Instrumentation Laboratory, Inc., April 1979.

Jurkowski, J.E., Jones, N.L., Walker, W.C., Younglai, E.V., & Sutton, J.R. Ovarian hormone response to exercise. Journal of Applied Physiology, 1978, 44, 109-114.

Keizer, H.A., Poortman, J., & Bunnik, G.S.J. Influence of physical exercise on sex hormone metabolism. Journal of Applied Physiology, 1980, 48 (5), 765-769.

Kerlinger, F.N., & Pedhazur, E.J. Multiple regression in behavioral research. New York: Holt, Rinehart & Winston, Inc., 1973.

Kilbom, Å. Physical training in women. Scandinavian Journal of Clinical Laboratory Investigation (Supplement 119), 1971, 28, 1-31.

Kollis, J., Bartlett, H.L., Oja, P., & Shearburn, C.L. Cardiac output of sedentary and physically conditioned women during submaximal exercise. Australian Journal of Sports Medicine, 1977, 9, 63-68.

Kreitzman, S. Nutritional assessment score for evaluation of dietary adequacy. Atlanta, Georgia: Center for Nutrition and Dental Health, Emory University (unpublished), 1981.

Labovitz, S. Criteria for selecting a significance level: A note on the sacredness of .05. The American Sociologist, 1968, 3, 220-225.

Lamb, D.R. Physiology of exercise: Responses and adaptations. New York: Macmillan Publishing Company, Inc., 1978.

Larsson-Cohn, V. The length of the first three menstrual cycles after combined oral contraceptive treatment. Acta Obstetrica and Gynecologica Scandinavica, 1969, 48, 416-419.

Lopez, S.A., Vial, R., Balart, L., & Arroyave, G. Effect of exercise and physical fitness on serum lipids and lipoproteins. Atherosclerosis, 1974, 20, 1-9.

Lutter, J., & Cushman, S. The diversity of menstrual patterns among women runners. The Physician and Sportsmedicine (accepted for publication, February 1982), in press.

MacArthur, 1.W., Bullen, B.A., Beitins, I.Z., Pagona, M., Bagner, T.M., & Klibanski, A. Hypothalamic amenorrhea in runners of normal body composition. Endocrine Research Communication, 1980, 7 (1), 13-25.

Mann, G.V., Garrett, H.L., Farhi, A., Murray, H., & Billings, F.T. Exercise to prevent coronary heart disease. American Journal of Medicine, 1969, 46, 12-23.

Mayhew, J.L., & Gross, P.M. Body composition changes in young women with high resistance weight training. Research Quarterly, 1974, 56, 433-440.

Miller, N.E., Rao, S., & Lewis, B. High density lipoprotein and physical activity. Lancet, 1979, 1, 111-116.

Miller, T. Life events scaling: Clinical methodological issues. Nursing Research, 1981, 30 (5).

Moody, D.L., Kollias, J., & Buskirk E.R. The effect of a moderate exercise program on body weight and skinfold thickness in overweight college women. Medicine and Science in Sports, 1969, 1, 75-80.

Morehouse, L.E. Laboratory manual for physiology of exercise. St. Louis: The C.V. Mosby Company, 1972.

Mountcastle, V.B. (Ed.). Medical physiology. St. Louis: The C.V. Mosby Company, 1980.

Penny, G.D. Heart rate, blood pressure, serum lactate and serum cholesterol changes after cessation of training. Journal of Sports Medicine and Physical Fitness, 1975, 15, 223-28.

Petterson, F., Fries, H., & Nillus, S.J. Epidemiology of secondary amenorrhea. American Journal of Obstetrics and Gynecology, September 1973, 80-86.

Pollock, M.L. The quantification of endurance training programs. In J.H. Wilmore (Ed.), Exercise and sports science reviews. New York: Academic Press (Vol. 1), 1973, pp. 155-188.

Rochelle, R. Blood plasma cholesterol changes during a physical training program. Research Quarterly, 1961, 32, 528-550.

Roundy, E.S., Fisher, G.A., & Anderson, S. Effects of exercise on serum lipids and lipoproteins. Cardiology Clinics, 1978, 6.

Ruch, T., & Patton, H.D. (Eds.). Physiology and biophysics. Philadelphia: W.B. Saunders Company, 1979.

Rutkowski, R.B. Manual HDL-cholesterol procedure. Atlanta, Georgia: Grady Memorial Hospital Clinical Chemistry Laboratory, 1979.

Ryan, A.J., & Allman, F.L., Jr. (Eds.). Sports medicine. New York: Academic Press, 1974.

Schwartz, B., Rebar, R.W. & Yen, S.S. Amenorrhea and long distance running. Fertility and Sterility, 1980, 34, 306.

Shangold, M. Sports and menstrual function in the female. Physician and Sportsmedicine, 1980, 8, 66-70.

Shangold, M., Freeman, R., Thysen, B., & Gatz, M. Relationship between long-distance running, plasma progesterone and luteal phase length. Fertility and Sterility, 1979, 31, 130-134.

Shangold, M., Gatz, M.L., & Thysen, B. Acute effects of exercise on plasma concentrations of prolactin and testosterone in recreational women runners. Fertility and Sterility, 1981, 35, 699-704.

Sloan, A.W., Burt, J.J., & Blythe, C.S. Estimation of body fat in young women. Journal of Applied Physiology, 1962, 17, 967-970.

Siiteri, P.K. & Febres,J. Reproductive function in the female. Endocrinology. New York: Grunne and Stratton, 1980.

Speroff, L. & Redwine, D.B. Exercise and menstrual function. Physician and Sportsmedicine, 1980, 8, 42-48.

Sutton, J.R., Coleman, M.J., Casey, J., & Lazarus, L. Androgen responses during physical exercise. British Medical Journal, 1973, 1, 520-523.

Taylor, H.L. Relationship of physical activity to serum cholesterol concentration. In Rosenbaum & Balknop (Eds.), Work and the Heart. New York: Haeber, 1959.

Taylor, H.L., Anderson, J.J., & Keys, A. Studies on diet, physical activity and serum cholesterol concentration. Circulation, 1967, 24, 1055-1058.

Tepperman, J. Metabolic and endocrine physiology. Chicago: Yearbook Medical Publishers, 1980.

Trussel, J. Menarche and fatness: Reexamination of the critical body composition hypothesis. Science, 1978, 200, 1506-1508.

Vander, A.J., Sherman, J.H., & Luciano, D.S. Human physiology: The mechanics of body function. New York: McGraw Hill Book Company, 1980.

Vigersky, R.A., Anderson, A.E., Thompson, R.H., & Loriaux, D.L. Hypothalamic dysfunction in secondary amenorrhea associated with simple weight loss. New England Journal of Medicine, 1977, 297, 1141-1145.

Webb, M. Personal communication to Dr. Edwin Dale, 1981.

Weltman, A., Matter, S., & Stamford, B.A. Caloric restriction and/or mild exercise: Effects on serum lipids and body composition. American Journal of Clinical Nutrition, 1980, 33, 1002-1009.

Wentz, A.C. Body weight and amenorrhea. Obstetrics and Gynecology, 1980, 56 (4), 482-487.

Wentz, A.C., Jones, G.S., & Sapp, K. Pulsatile gonadotropin output in menstrual dysfunction. Obstetrics and Gynecology, 1976, 47, 309-312.

Williams, R.H. (Ed.). Textbook of endocrinology. Philadelphia: W.B. Saunders, 1980.

Wilmore, J.H. Alterations in strength, body composition and anthropometric measurements consequent to a 10-week training program. Medicine and Science in Sports, 1974, 6, 133-138.

Wilmore, J.H., & Brown, C.H. Physiological profiles of women distance runners. Medicine and Science in Sports, 1974, 6, 178-181.

Wood, P., Haskell, W., Klein, H., Lewis, S., Stern, M.P., & Farquhar, J.W. The distribution of plasma lipoproteins in middle-aged male runners. Metabolism, 1976, 25, 1249-1257.

Wood, P.D., Haskell, W.L., Stern, P., Lewis, S., & Perry, C. Plasma lipoprotein: Distribution in male and female runners. Annals of the New York Academy of Sciences, 1977, 63, 748-763.

Wright, K., Collins, D.C., Mussey, P.I., & Preedy, J.R.K. A specific radioimmunoassay for estrone sulfate in plasma and urine without hydrolysis. Journal of Clinical Endocrinology and Metabolism, 1978, 47, 1092-1098.

Yaeger, S.A., & Brynteson, P. Effects of varying training periods on the development of cardiovascular efficiency of college women, Research Quarterly, 1970, 41, 589-592.

Yen, S. Neuroendocrine regulation of the menstrual cycle. Hospital Practice, 1979, 83-97.

Yen, S.S.C., Rebar, R., Vandenberg, G., & Judd, H. Hypothalamic amenorrhea and hypogonadotropinism: Responses to synthetic LRF. Journal of Clinical Endocrinology and Metabolism, 1973, 36, 811-814.

Zacharias, L., Wurlman, R., & Schatzoff, M. Sexual maturation in contemporary American girls. American Journal of Obstetrics and Gynecology, 1970, 108, 833-846.